

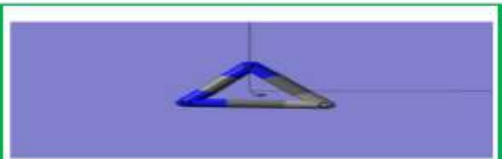


# Journal of Applicable Chemistry

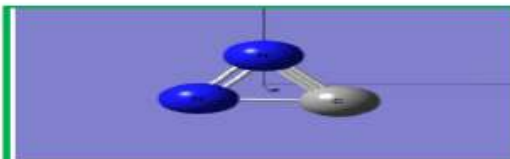
2024, 13 (3): 333-429  
(International Peer Reviewed Journal)



**New Chemistry News**  
**N=C=N**



**New News of Chem (NNC)**



**ChemNewsNew (CNN)**

**...CNN - 61b...I am ...**  
**...Intelligence Augmented Medicine...**  
**Cardiology**  
**Fits (Figure Image Table Script ...)Base**

Information Source	sciencedirect.com;ACS.org ;	
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**Conspectus:** “Intelligence Augmented Medicine (I am)” is broadly spread over human health care procedures viz. diagnosis of diseases, gold-standard-confirmation-tests, therapeutics, drug-administration, intervention procedures, surgery (pre-operative, intra-operative and post-operative chores), prognosis, relapse/recurring of the disease, and analysis of morbidity/mortality/bio-chemical/medico-chemical data. The important disciplines of concern are Cardiology, Neurology, Surgery, Anaesthesiology, Pulmonology, Gynaecology, Venereology, Urology, Hepatology, Ophthalmology, Dermatology, Oncology etc.

The present news-item “Fits.Cardiology” contains numerical/categorical demographic data of patients, images generated by medical-instruments, clinical/bio-marker tests/knowledge bits for consolidation of disease. This phase followed by moving for therapeutic treatment with drugs, intervention procedures,

repair/replacement of heart-valves etc.

**Keywords:** Artificial intelligence (AI); Medical diagnosis; Cardiology; Drug therapy; Life style change; Intervention, Surgery ;

Fits : [Figure Image Table Script;]

CNN : [C [Computations; Computer; Chemistry] NN [New News; News New; Neural Nets; Nature News; News of Nature;] ]

## Artificial Intelligence (AI)

Two AI winters and  
One Hot AI summer



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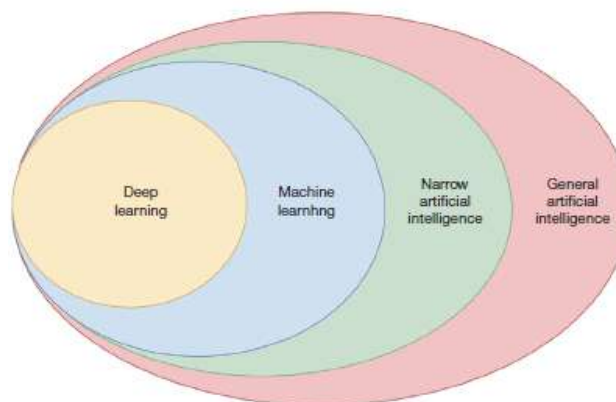


Evolving AI

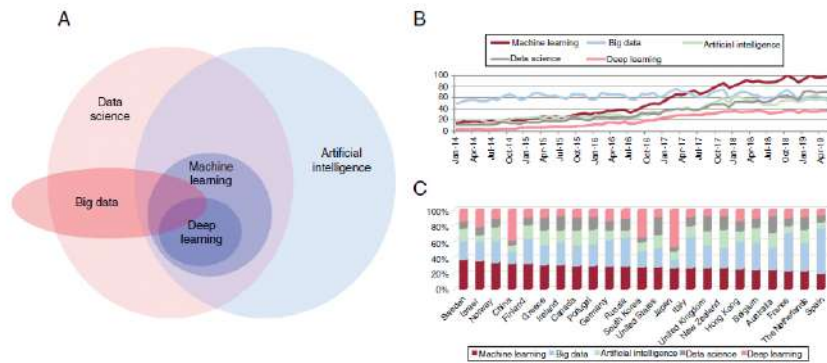


AI policy

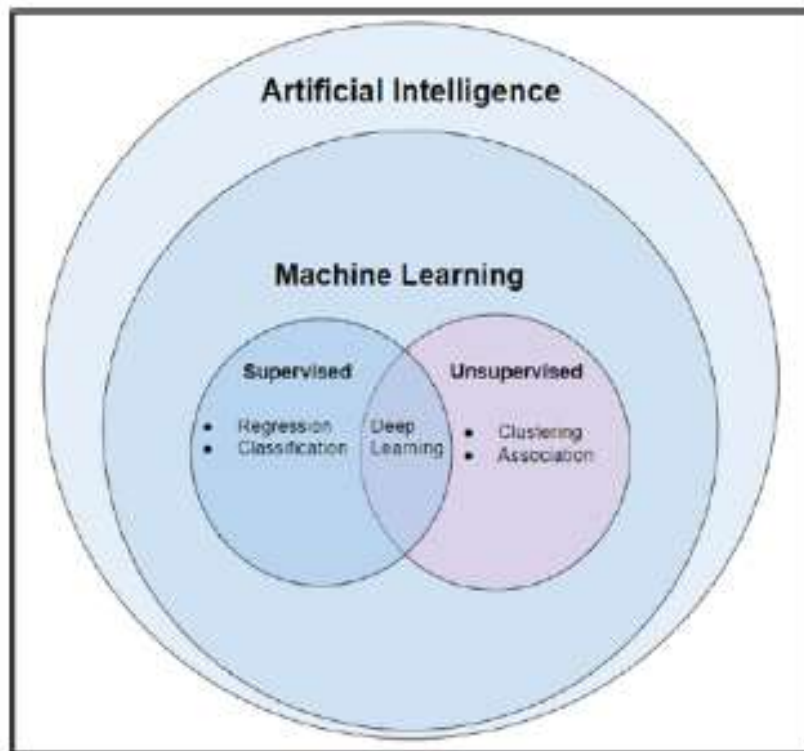
15



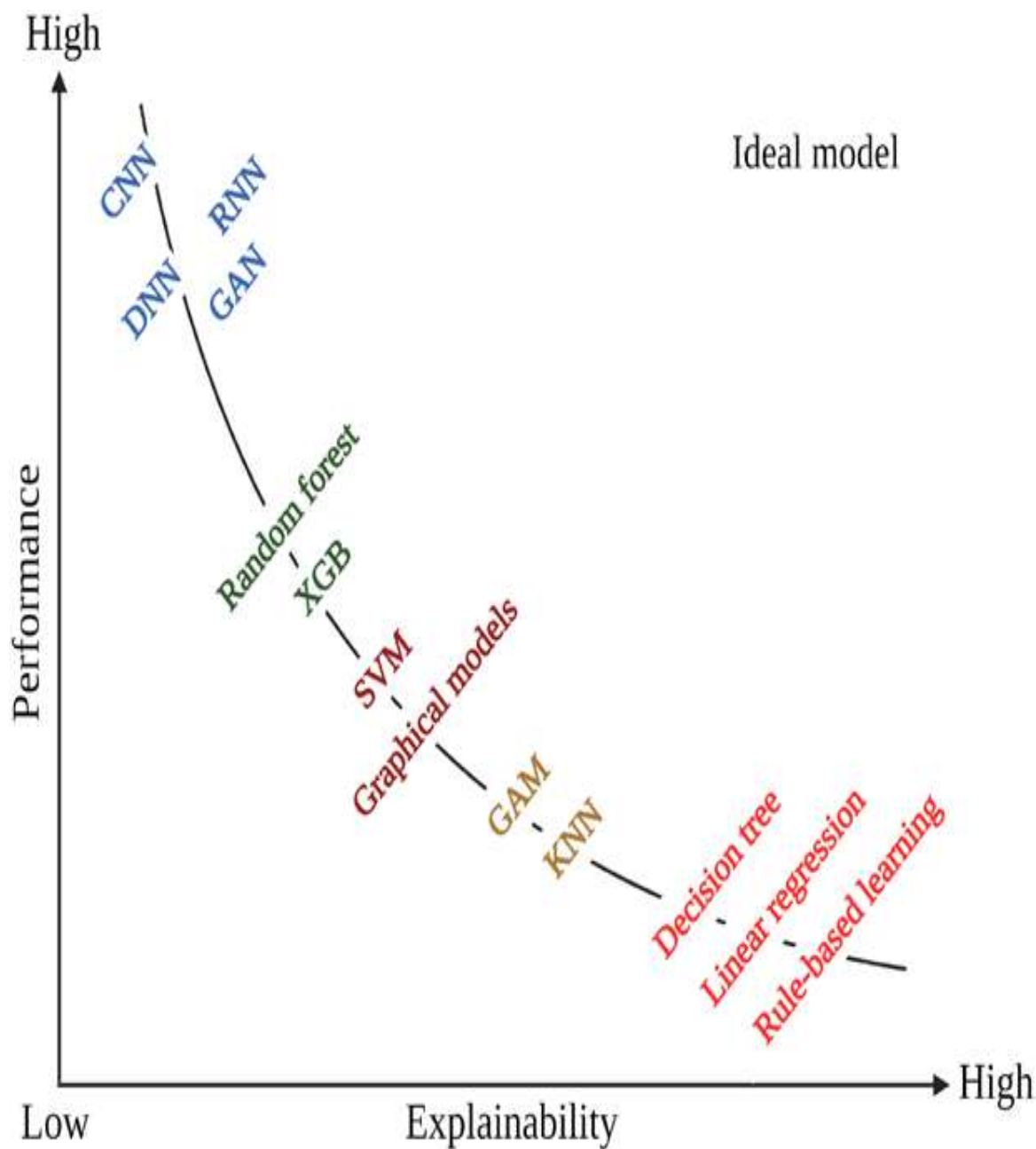
General AI, narrow AI, ML and DL



- 🔔 A: Venn Diagram of the most commonly used terms in the data science disciplines.
- 🔔 B: total searches (source: Google Trends) in the last 5 full years of terms related to artificial intelligence and data science; vertical axis : proportion of a topic with respect to the total number of searches on the topics.
- 🔔 C: the most searched term in each country in the same period



Venn diagram of the different approaches falling under the category of AI



Model explainability versus performance for some

Graphical models: probabilistic model such as Bayesian network. Rulebasedlearning: any model uses rules (eg, if:then) to make a decision.

CNN indicates convolutional neural network; DNN, deep neuralnetwork;

GAM, generalized additive model; GAN, generative adversarialnetwork;

KNN, K-nearest neighbor;

RNN, recurrent neural network;

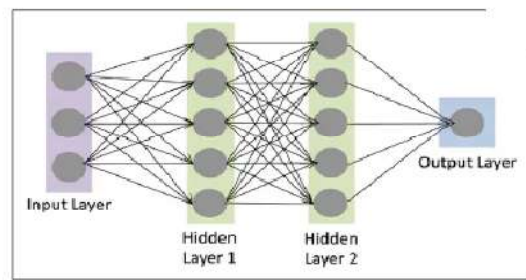
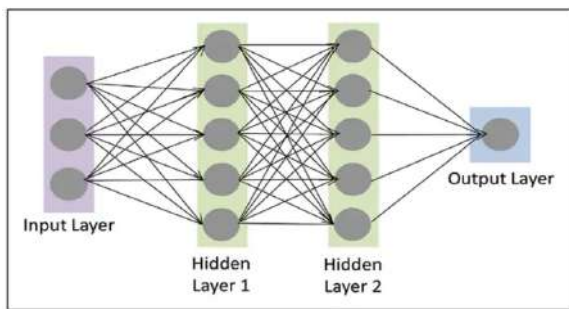
SVM, support vector machine; and XGB, extreme gradient boosting

**TABLE 1** Commonly Used Terms in AI

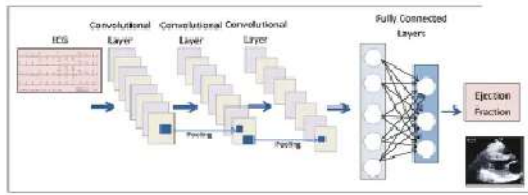
AI	A branch of applied computer science wherein computer algorithms are trained to perform tasks, and have the capability to imitate intelligent human intelligence.
ML	Subfield of AI, a machine learns to perform a task or make decisions automatically from an available data source without being explicitly programmed.
DL	DL is a type of ML that mimics the operation of the human brain and includes a class of algorithms called neural networks.
NLP	NLP is an area of computer science and artificial intelligence related to the organization of unstructured narrative text into a structured form that can be interpreted by a machine and allows for automated information extraction.
Cognitive computing	Cognitive computing platforms integrate machine learning, reasoning, natural language processing, speech and object recognition, human-computer interaction, dialog and narrative generation.
Computer vision	Computer vision is a branch of computer science concerned with objects and feature recognition in images or multi-dimensional data, including digital video frames.
Robotics	Robotics deals with the design, construction, operation, and use of robotic devices that can move and react to sensory input. Robotics also concerned with creation of computer systems for their control, sensory feedback, and information processing.
AI = artificial intelligence; DL = deep learning; ML = machine learning; NLP = natural language processing.	

# NNs

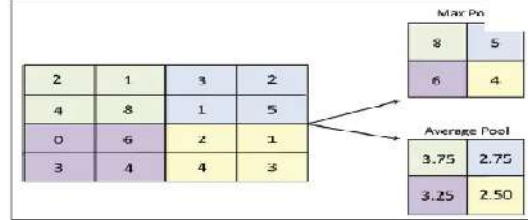
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**Recurrent neural network**



Convolutated neural network

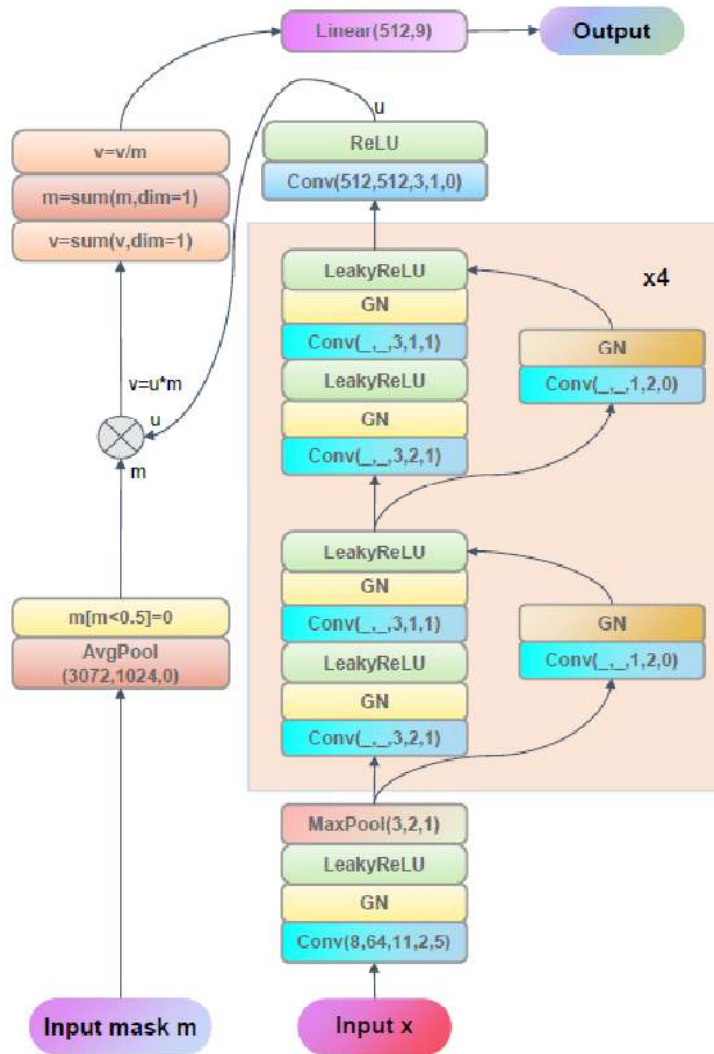


Pooling examples

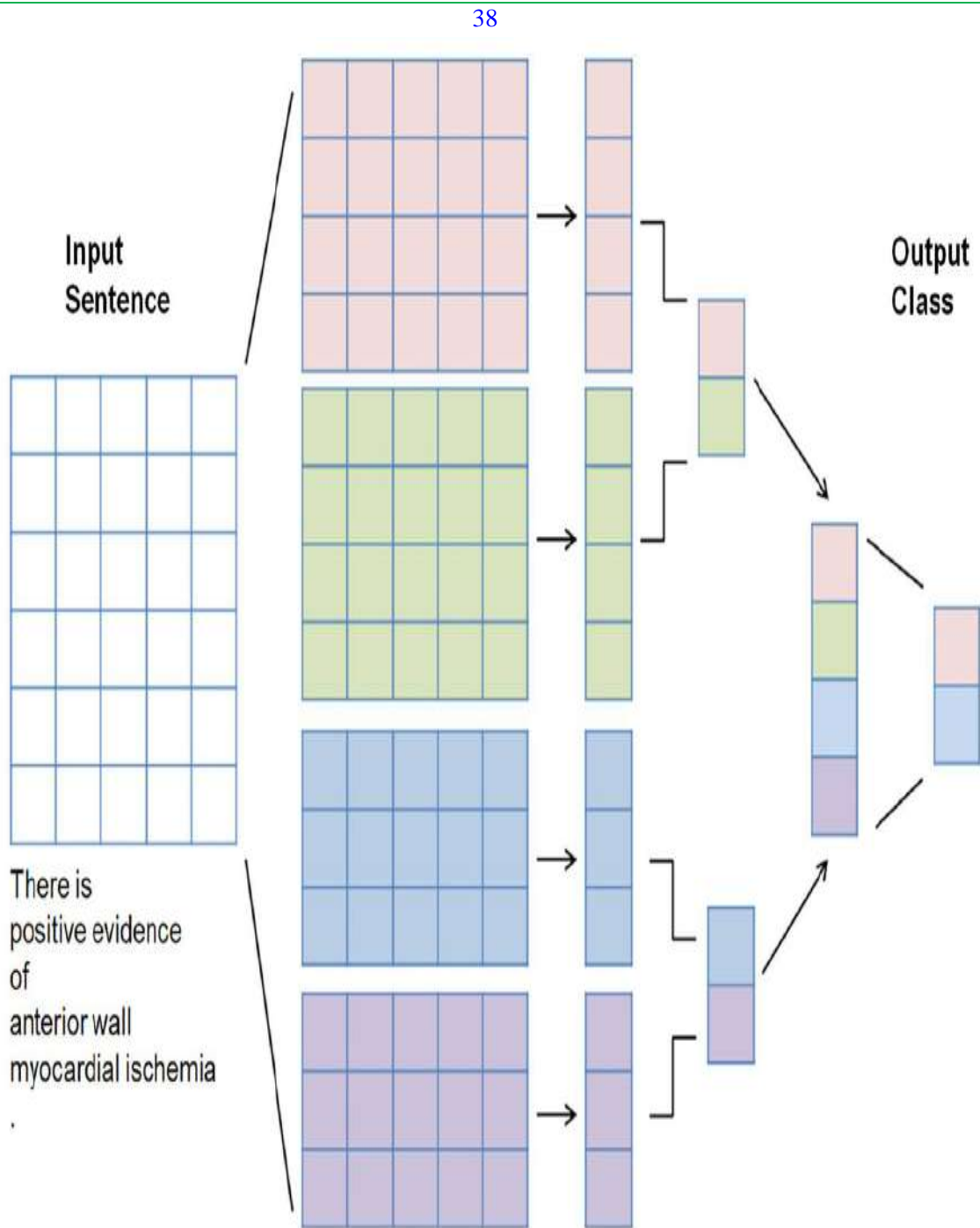
# CNN

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## High-level architecture of CNN



- ✓ Size of the input mask is the same as the size of the input x.
- ✓ Mask will help the network ignore the padded zero elements in x, which has a variable length.
- ✓ Network outputs the classification scores



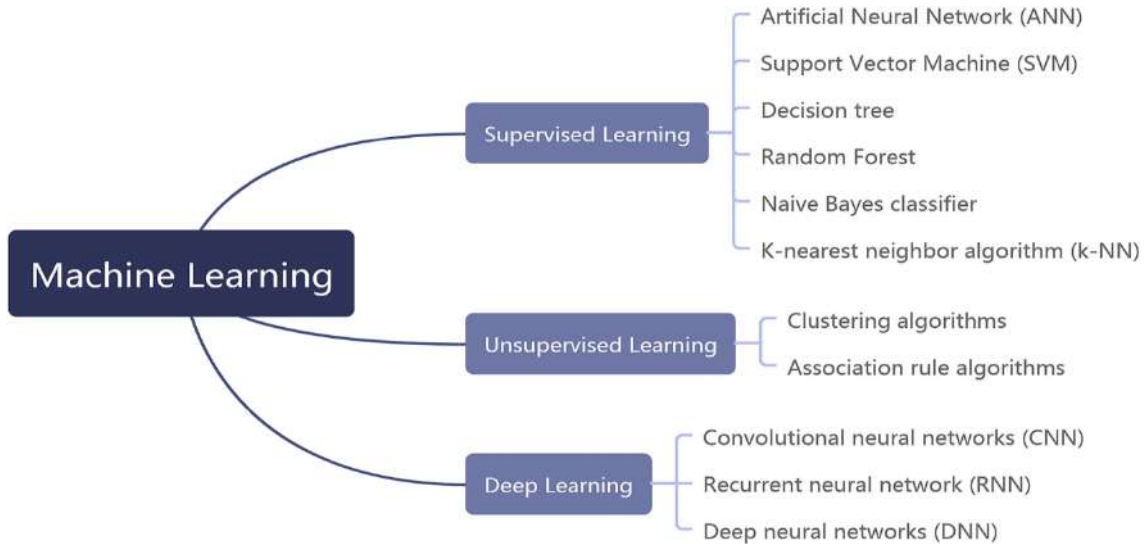
**Deep learning CNNs for diagnostic classification.**

- ✓ Diagram of a CNN model. It converts an **input sentence** (through several convolutions), into two output classes: **positive diagnosis or negative diagnosis**



# Machine Learning (Mach.Lrn)

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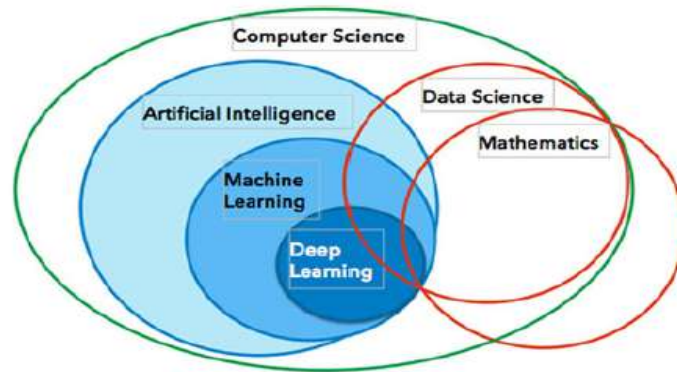
## Types of Learning Data based

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Types of Machine Learning

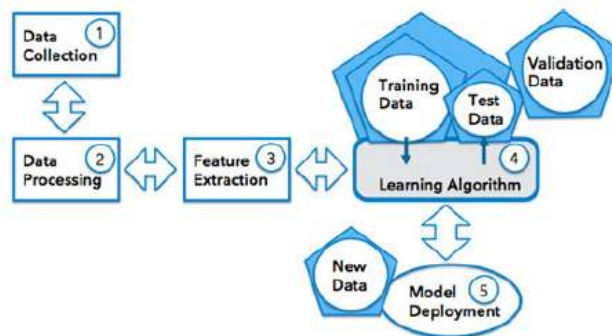
Supervised learning	Unsupervised learning	Reinforcement learning
Machine learns explicitly	Machine understand the data	Machine learns how to act in certain environment
Labeled data with clearly defined inputs	Inputs only	Focus on making decision based on previous experience
Predicts outcome/future	Labels and output unknown	Reward based learning with positive and negative feedback
Resolves classification and regression problems	Identify patterns or structure	Optimization of treatment policies
Risk of mortality, readmission prediction	Novel classification of diseases	Real-time decisions
Image Classification	Big data visualization	Robot navigation
Diagnostics	Image feature elicitation and segmentation	

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- ✓ Artificial intelligence algorithms are built from big data, and data mining and data science are incorporated.
- ✓ The main branch of artificial intelligence is machine learning and its subtype deep learning.
- ✓ Ref: Chang AC. Artificial Intelligence in Medicine: Principles and Applications. Elsevier; 2020,

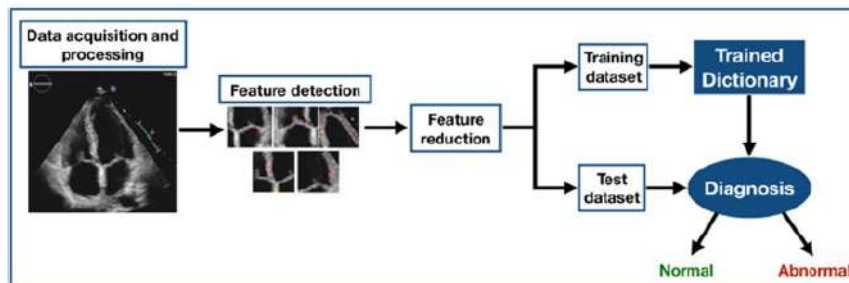
34



The machine learning workflow

- 🔔 Data collection, data processing, feature selection and algorithmic development.
- ✓ Ref: Chang AC. Artificial Intelligence in Medicine: Principles and Applications. Elsevier; 2020

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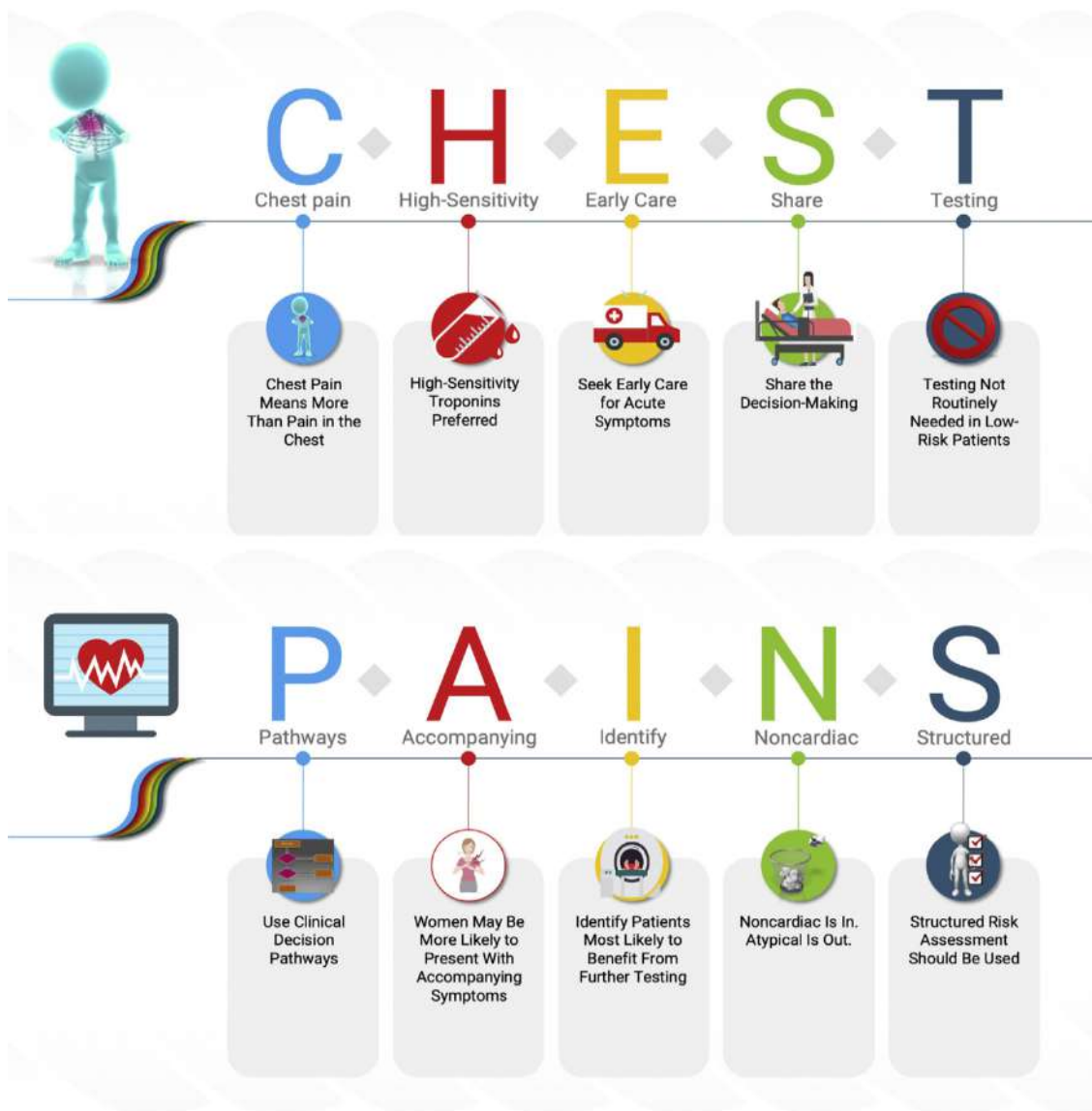


- ✓ An example of a convolutional neural network.
- ✓ Ref: Alsharqi, et al. Echo Res Pract. 2018;5:R115–R125

# Cardiology (Cardia)

## Chest pain

24



Take-Home Messages for the Evaluation and Diagnosis of Chest Pain


# AI +cardiology

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## Artificial intelligence and cardiology – a marriage made in heaven or in hell ?

**HOPE ? HEAVEN ?**


1. AI outperforms humans
2. AI will democratise cardiovascular knowledge
3. AI is the only way to handle multimodal big data
4. AI will redefine cardiovascular disease
5. AI can recognise and mimic human emotions



**HYPE ? HELL ?**

1. Computers cannot be intelligent
2. AI is not the objective
3. Current AI tools are only as good as experts
4. Earlier and more precise diagnosis is not necessarily better
5. Regulation is proposed because risks have been recognised

14,436  
in 2020



PubMed literature with machine learning (ML) and AI

04

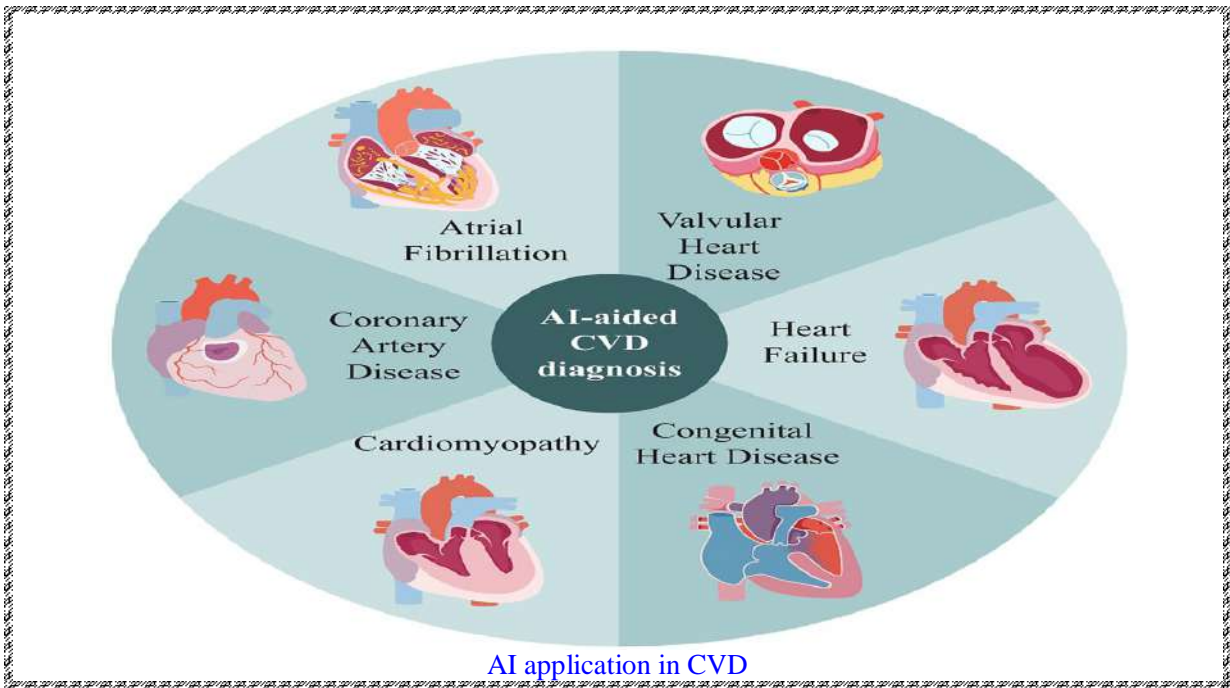
## AI in cardiology



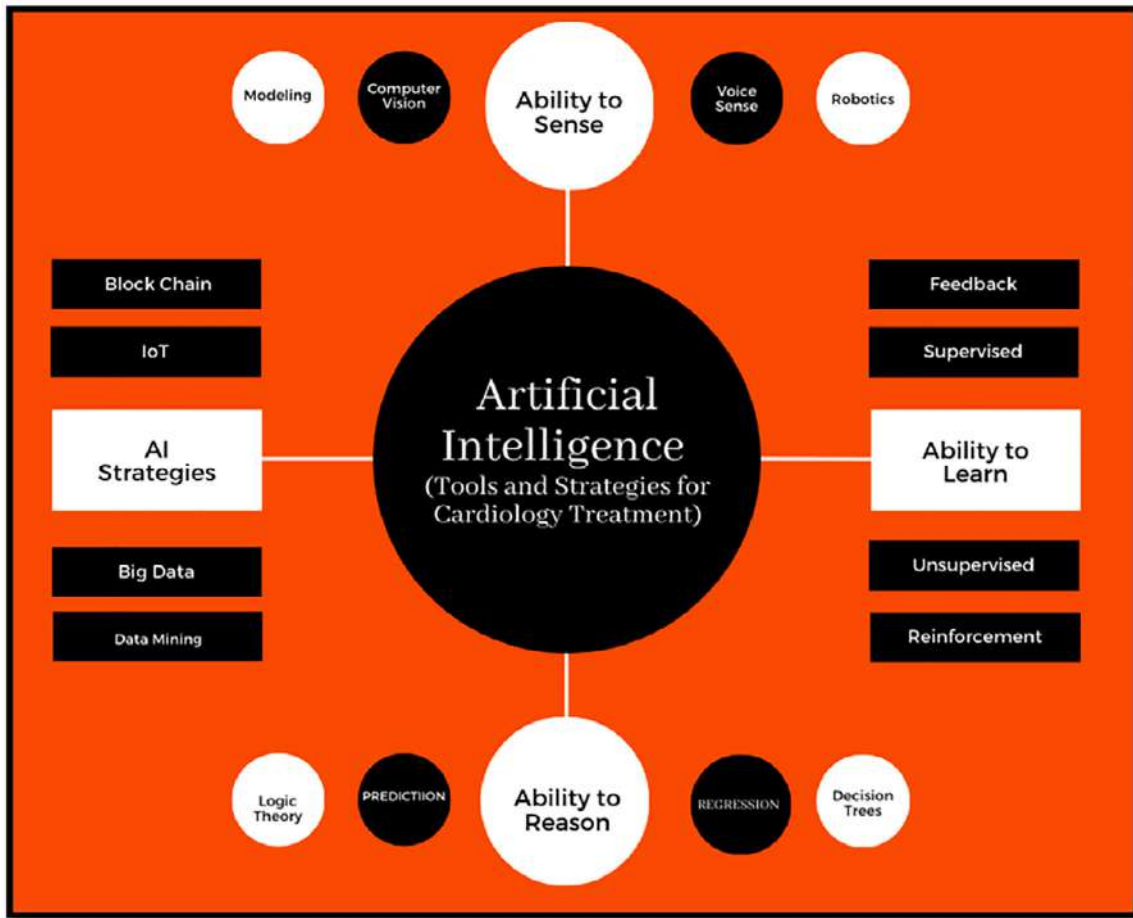


Alin Imaging (New ACR AIcentral.org)

# AI +cardiology Diagnosis



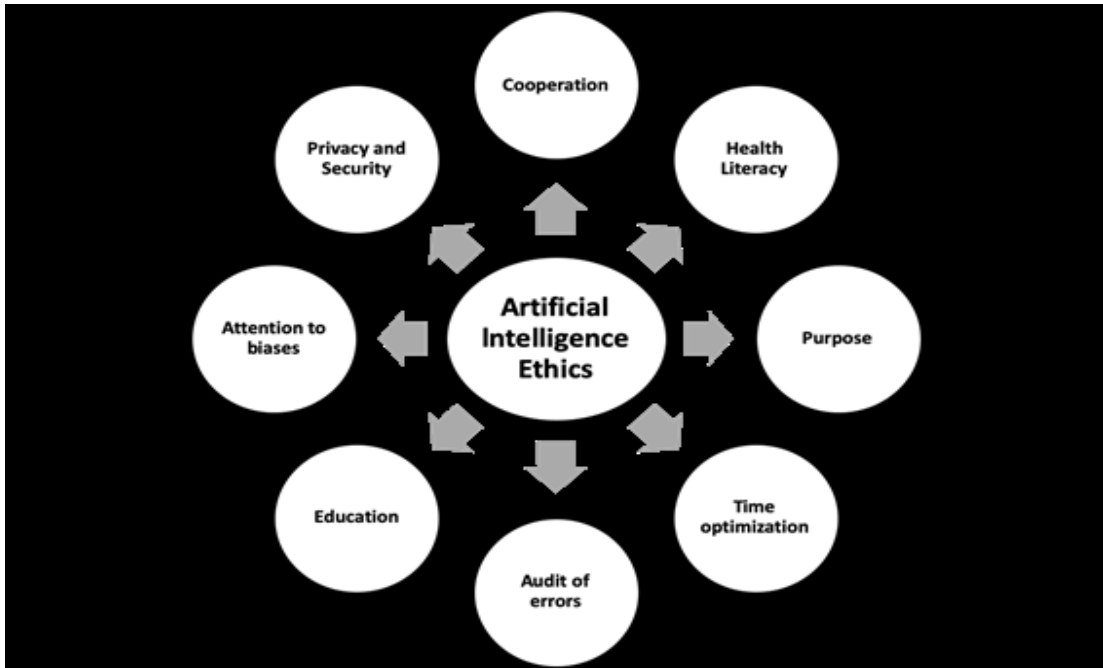
AI application in CVD



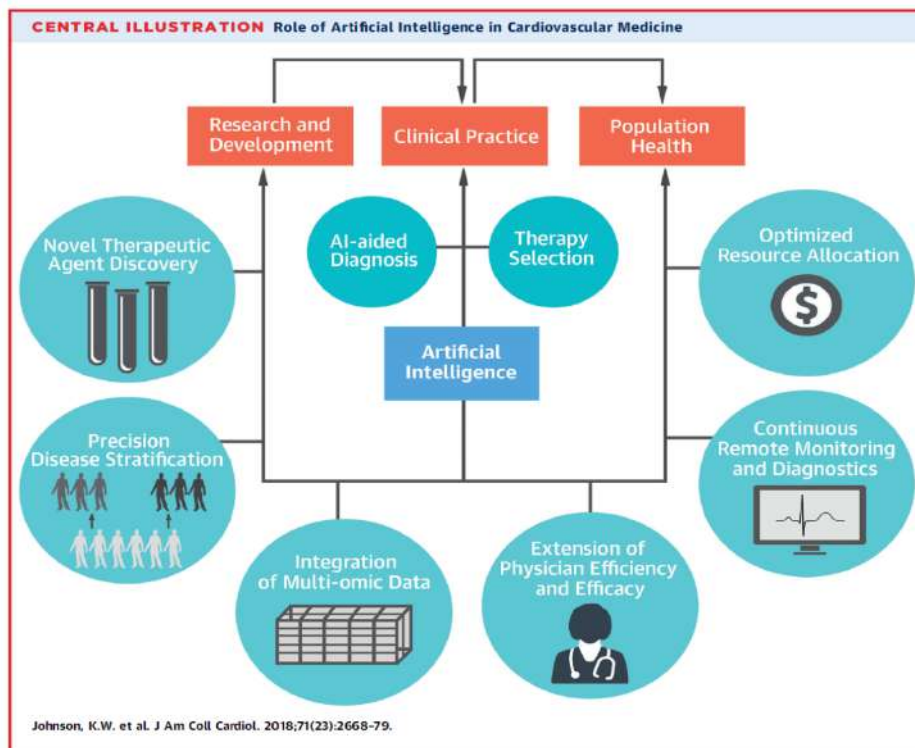
Tools and strategies of Artificial Intelligence for cardiology during COVID-19.

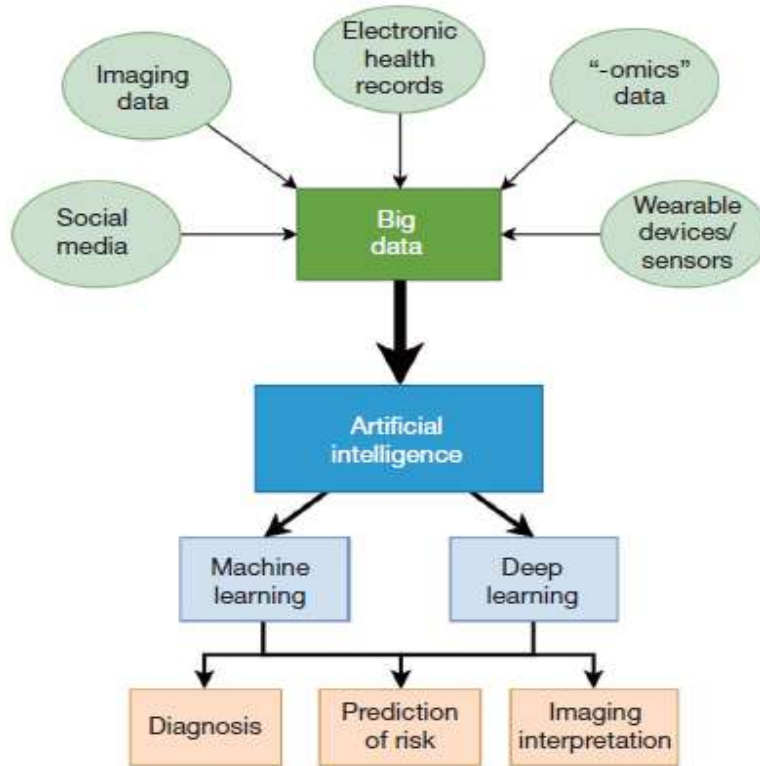


Features and solicitations of Artificial Intelligence during COVID-19



AI implementation in clinical practice considering ethics



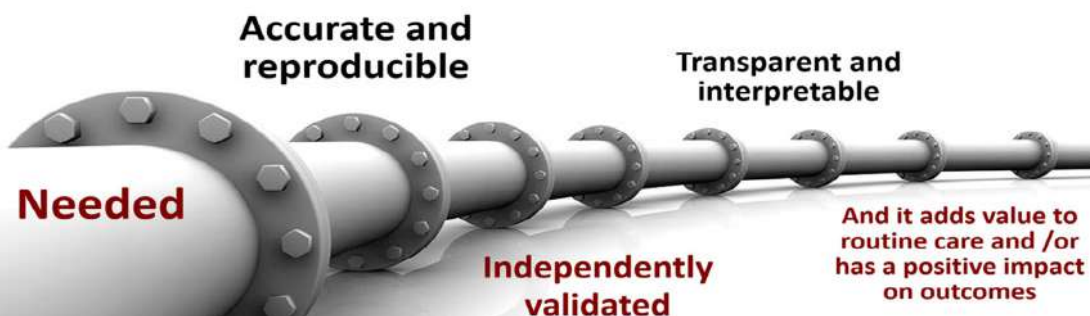


Information flow and inter-links between various data sources

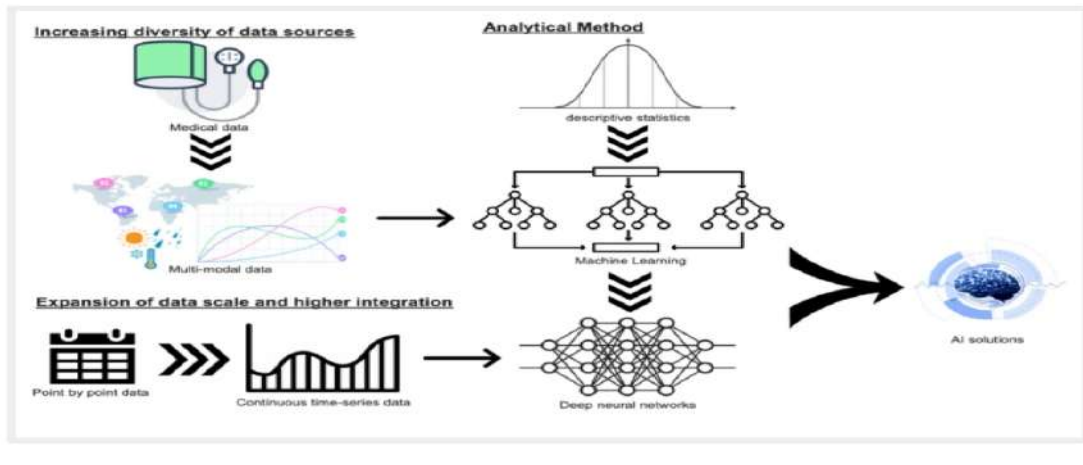
## AI. machine learning (Mach.Lrn ,ML) +cardiology

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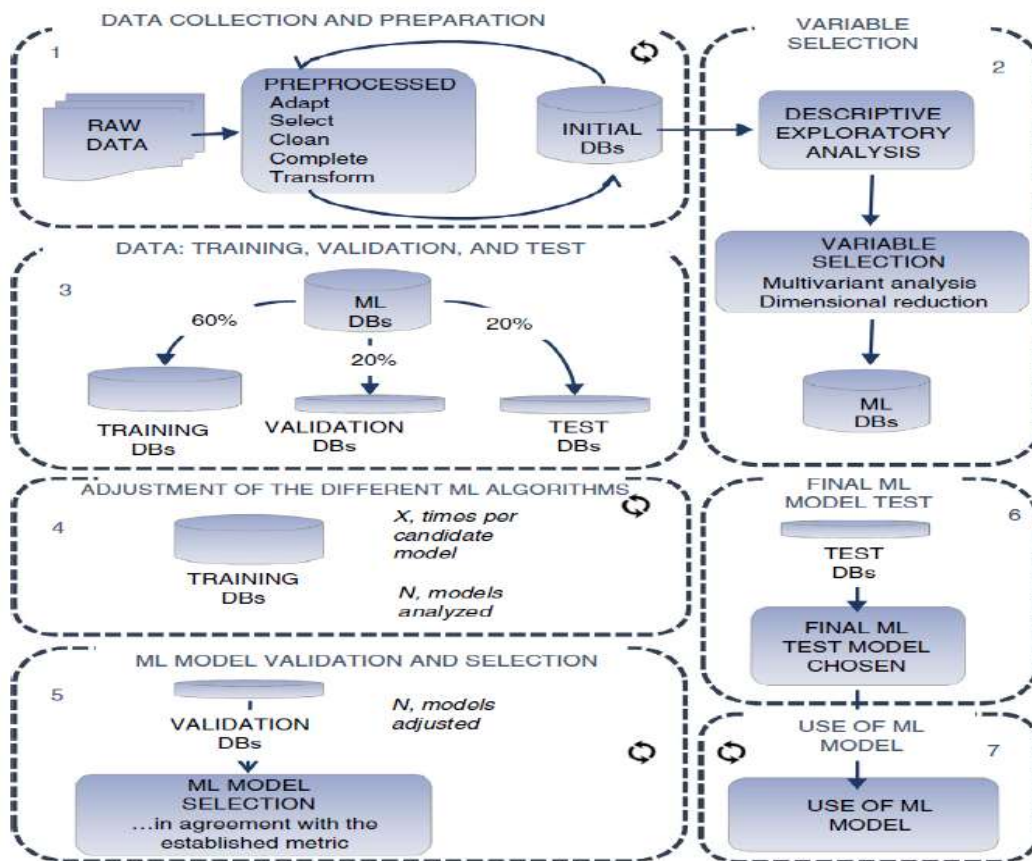
Machine learning will be implemented in clinical practice  
when it is feasible and trustworthy and if it is ..





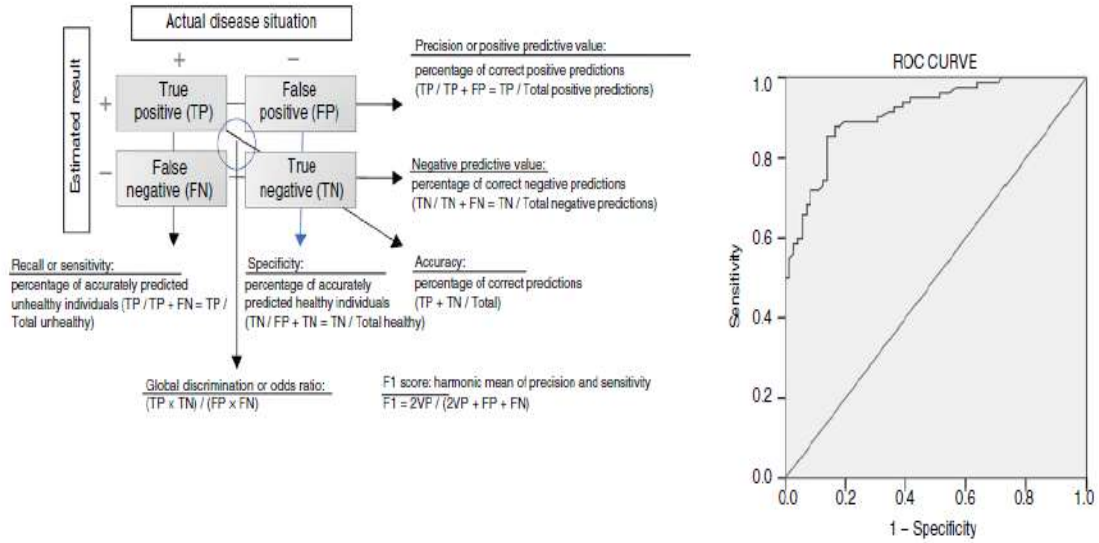


Recent developments in machine learning modeling methods for hypertension treatment  
 Hirohiko Kohjitani, Hiroshi Koshimizu, Kazuki Nakamura and Yasushi Okuno  
 Hypertension Research 47, 700–707 (2024)



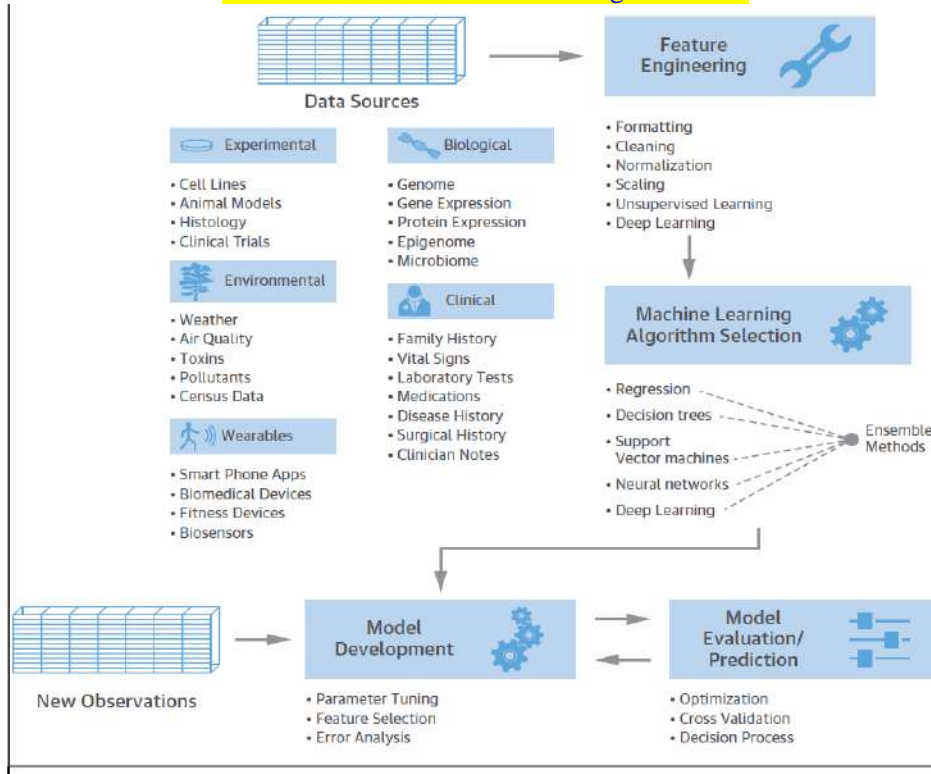
Application methodology of a machine learning (ML) model.

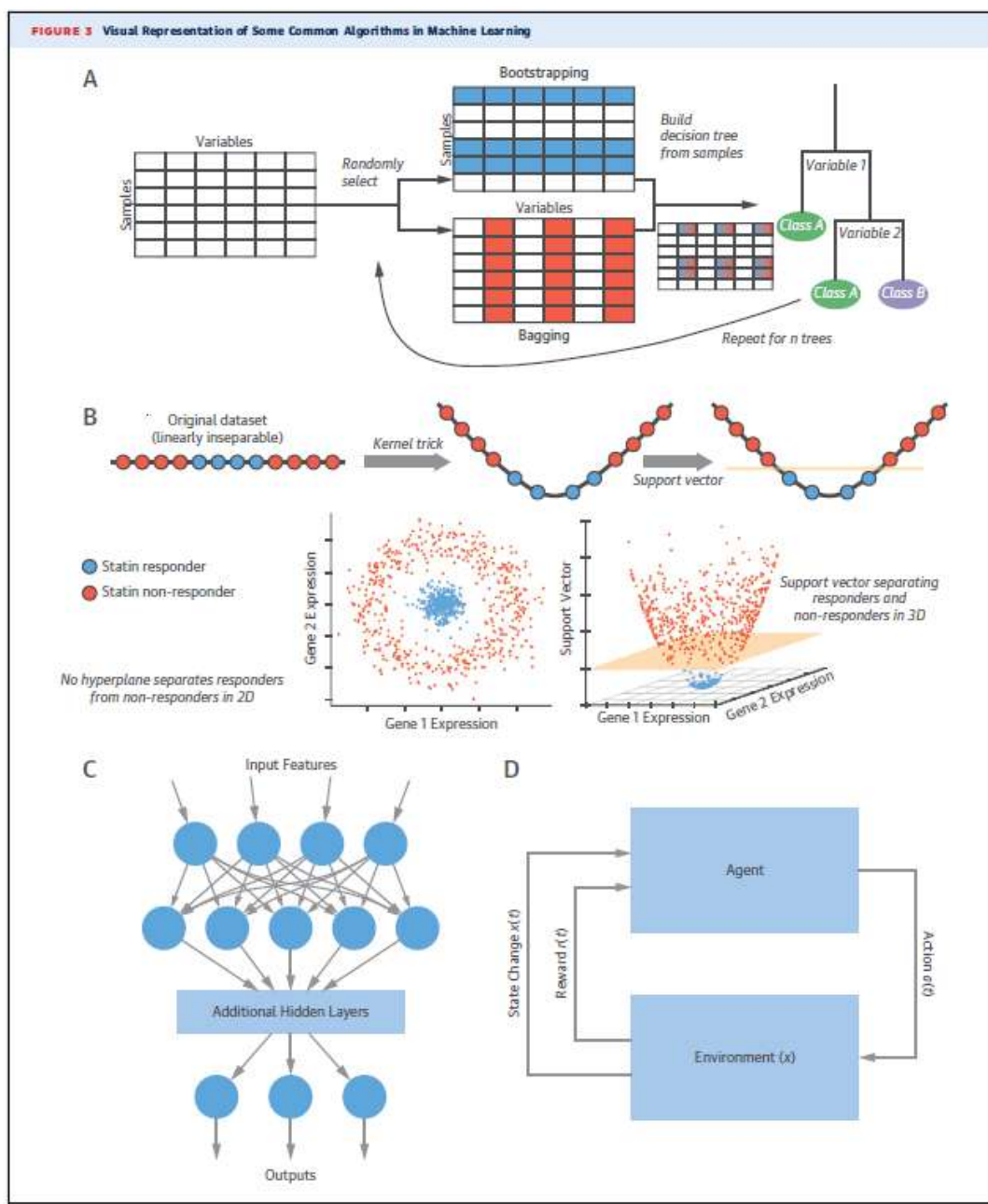
DB, database;



Metrics commonly used to evaluate supervised classification algorithms

Overview of the Machine Learning Workflow



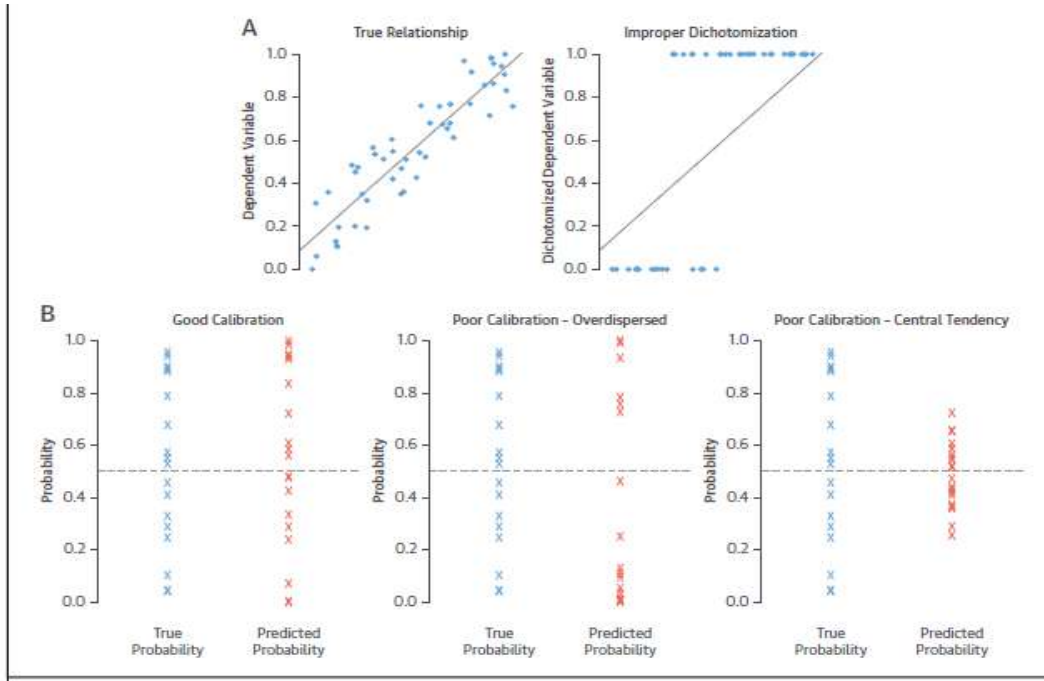


(A) Random forests : (incorporate both bootstrapping [selection of a subset of samples] and bagging [selection of a subset of predictive variables] for each individual tree.

(B) Support vector machines. In binary classification, a support vector machine finds a hyperplane that separates classes. The “kernel trick” projects input data to a higher dimension before an ensuing support vector is computed.

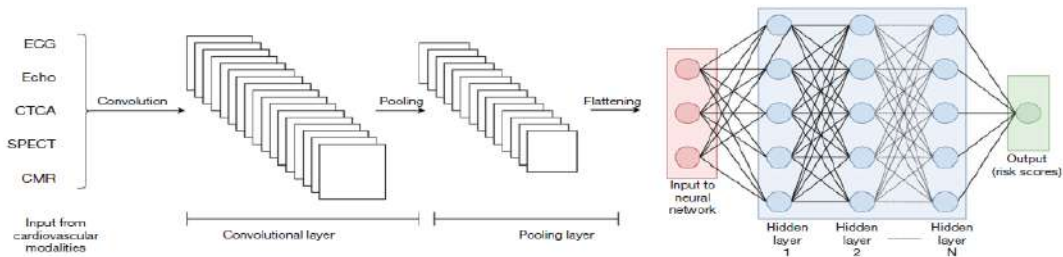
(C) Deep learning models comprise layers of stacked neurons that can be used to learn complex functions.

(D) Reinforcement learning algorithms are used to train the action of an agent on an environment



- ✓ (A) Visual demonstration of the concept of improper dichotomization on a dependent variable.
  - Improper dichotomization obfuscates continuous relationships between predictors and response variables.
- ✓ (B) Concept of “calibration” in predicted probabilities in a supervised learning model.
  - Because many machine learning tasks are framed as binary classification, the calibration of predicted probabilities is often underappreciated.
  - Proper calibration of predicted probabilities is often just as important as accurate binary classification because reduction of probabilities to binary classifications can be understood as a form of improper dichotomization

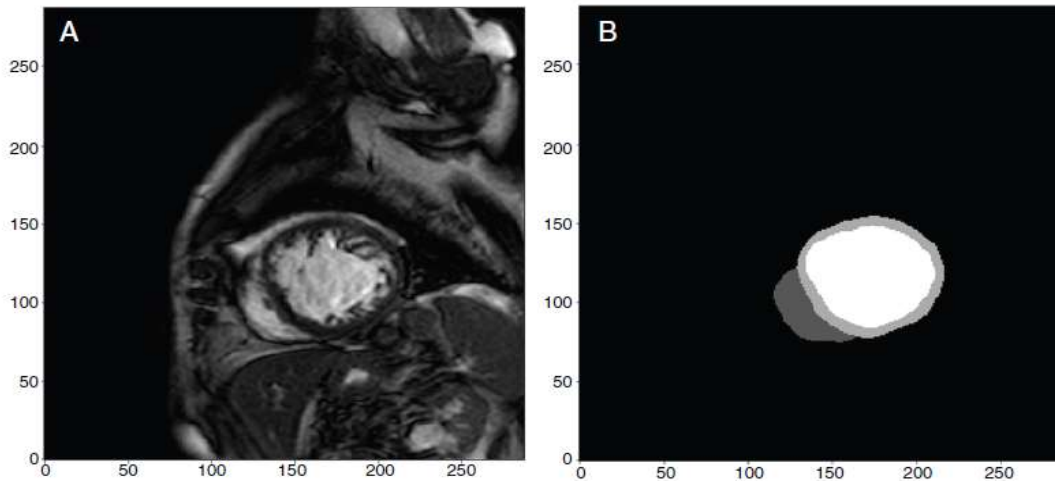
# CNN + Cardiology



Risk prediction and probability scores  
with a deep CNN with (N) hidden layers  
from medical instruments

# Segmentation and identification Cardiology

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Automatic segmentation and identification of the left and right ventricle

- ✓ Deep learning performed in our department from images obtained with a 1.5-T Philips Achieva resonance system.
- ✓ 12 original images

(A) Neural network identified and segment the left and right ventricles

(B) white color for the left ventricle, light gray color for the myocardium of the left ventricle, and dark gray color for the right ventricle

# AI +cardiology Table Format

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ML model	Description	Type of learning
SVM: support vector machine	Used for classification and regression purposes, it involves finding a hyperplane that best divides a dataset into different classes. A commonly used model in differentiating between different cardiac pathologies in echocardiography (4,13,14).	Supervised
RF: random forests	Consists of a large number of individual decision trees that operate ensemble (4,13,14).	Supervised
KL: kernel learning	Method of using linear classifiers to solve non-linear problems. Commonly used when combining cardiovascular data from different sources (4).	Unsupervised
CNN: convolutional neural network	Neural networks used to classify images, cluster images by similarity and perform object recognition. Consists of input and output layers separated by deep hidden layers (Figure 3).	Unsupervised or supervised

Application	ML model	Training dataset	Testing dataset
Differentiating between HCM & physiologic hypertrophy	SVM	–	139
	RF CNN		patients
Differentiating between HCM, cardiac amyloid and PAH	CNN	12,035 studies	8,666 studies
Differentiating between constrictive pericarditis & restrictive cardiomyopathy	SVM KL	–	94
	CNN RF		patients
Classifying still echo image captures into apical 2 chamber, apical 4 chamber and apical long-axis view	SVM KL	210 clips	99 clips
	RF CNN		
Classifying still echo image captures into 15 standard echo views	CNN	240 patients	27 patients
Classifying echo studies according to the ASE/EACVI diagnostic algorithm for diastolic dysfunction severity	CNN	6,182 studies	1,546 studies
Assessment of myocardial velocity	KL	–	55 patients
Detecting wall motion abnormality	CNN	–	61 patients
Quantifying MR	SVM	5,004 clips	–

🔔 SVM, support vector machine;  
🔔 RF, random forests;

🔔 HCM, hypertrophic cardiomyopathy;  
🔔 PAH, pulmonary arterial hypertension;  
🔔 MR, mitral regurgitation

Application	ML model	Training dataset (patients)	Testing dataset (patients)	AUC
Screening hyperkalemia from a 2-lead ECG in patients with CKD	CNN	449,380	61,965	0.88
Detecting asymptomatic LV dysfunction from a 12-lead ECG	CNN	44,959	52,870	0.93
Predicting AF in asymptomatic patients in sinus rhythm from a 12-lead ECG	CNN	126,526	54,396	0.90
Detecting LV hypertrophy from a 12-lead ECG	CNN	12,648	5,476	0.87
Predicting gender & age from a 12-lead ECG	CNN	499,727	275,056	0.94
Diagnosing arrhythmia from a single lead ECG	CNN	29,163	328	0.97
Detecting MI from a 12-lead ECG	CNN	–	290	–

- ✓ AF, atrial fibrillation; CKD, chronic kidney disease; LV, left ventricular; MI, myocardial infarction;
- ✓ ECG, electrocardiogram
- ✓ ML, machine learning; CNN, convolutional neural network; AUC, area under the curve

# Electronic health records (HER) in AI +cardiology

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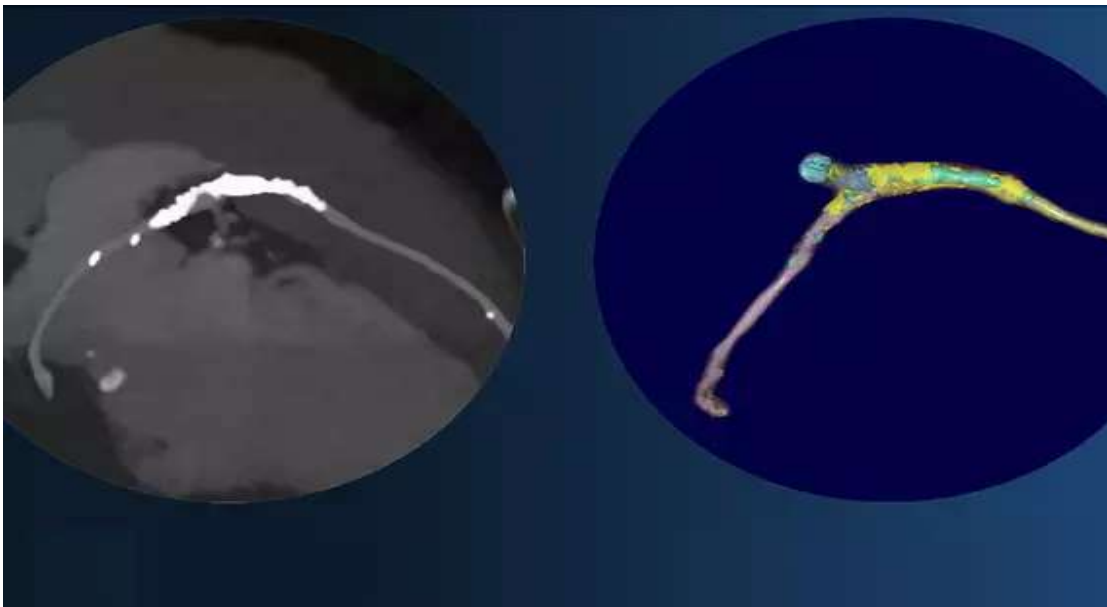
## Electronic health records (HERs)

Application	Training dataset (patients)	Testing dataset (patients)	AUC
Predicting non-hypertensive HF	700,000	76,214	0.87
Predicting MI	700,000	76,214	0.85
Predicting clinical deterioration on the wards (cardiac arrest, ICU transfer or death)	161,999	108,000	0.8
Predicting hospital re-admission within 30 days in HF patients	39,533 747	16,944 321	0.52 0.78
Predicting incidence of HF from EHR events	265,336	33,317	0.78

AUC, area under curve; HF, heart failure; MI, myocardial infarction; ICU, intensive care unit.

# Software for AI +cardiology

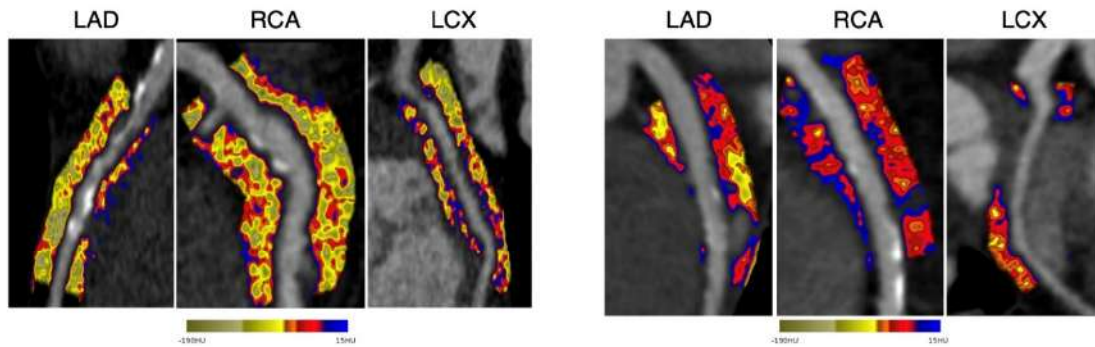
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Elucid's AI analysis software in action.

- ✓ Left image : coronary CT angiography of a vessel showing plaque heavy calcium burden.
- ✓ Right image: processed by Elucid's AI software,
  - highlights the various types of plaque morphology of these lesions

## Inflammation was the missing piece



Post-hoc CaRI-Heart analysis revealed patient had **low inflammation** (<50<sup>th</sup> centile in all vessels, compared with people of the same age and gender), indicative of **low disease activity**

Patient didn't experience any adverse event during 11-year follow-up

Post-hoc CaRI-Heart analysis revealed patient was at **very high relative risk**, with **high inflammation** in all arteries (above the 95<sup>th</sup> centile, compared with people of the same age and gender), indicative of **high disease activity**

Patient died of Myocardial Infarction due to proximal LAD occlusion 5 months later



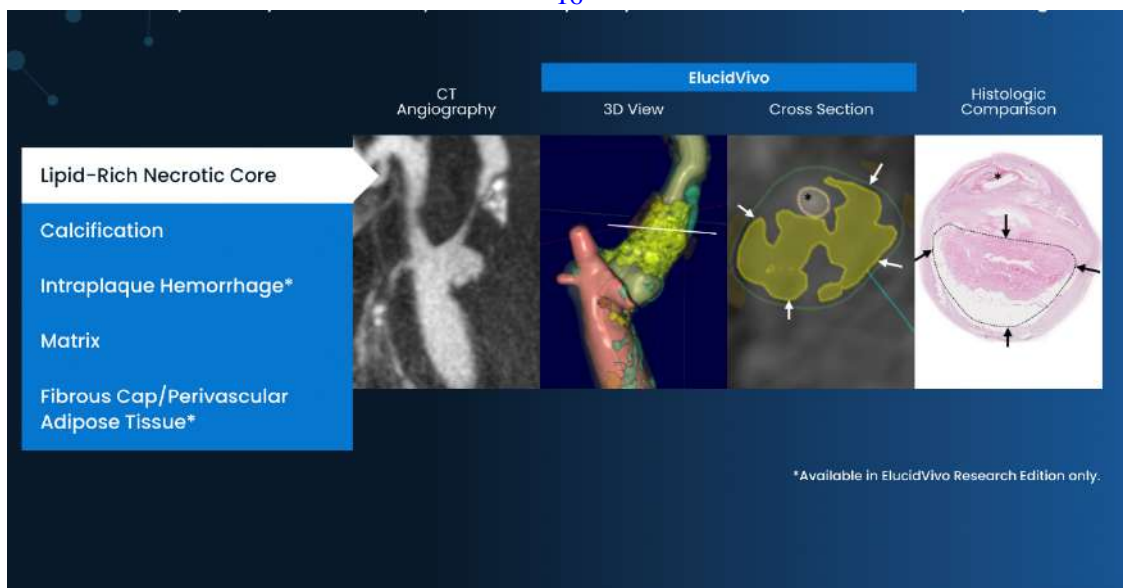
✓ One page from an AI report on the coronary plaque from patient's CTA scan.

- + FDA-cleared software developed Cleerly enables rapid soft plaqueAI assessment,
- + These types of reports may enable a new level of preventive care in cardiology,
  - o treating patients long before they have symptomatic disease
  - + Overcoming previously tedious and time consuming manual task of making these calculations





- ✓ AI-generated coronary tree from a patient's CT scan
  - + showing a color code of areas of interest for plaque burden from the Cleerly software shown at SCCT 2022.



Example of the CT image

- ✓ AI plaque assessment, cross section of a coronary plaque
- ✓ AI assessment and the matching histology for comparison from the same vessel segment from testing of the Elucid AI soft plaque analysis software.

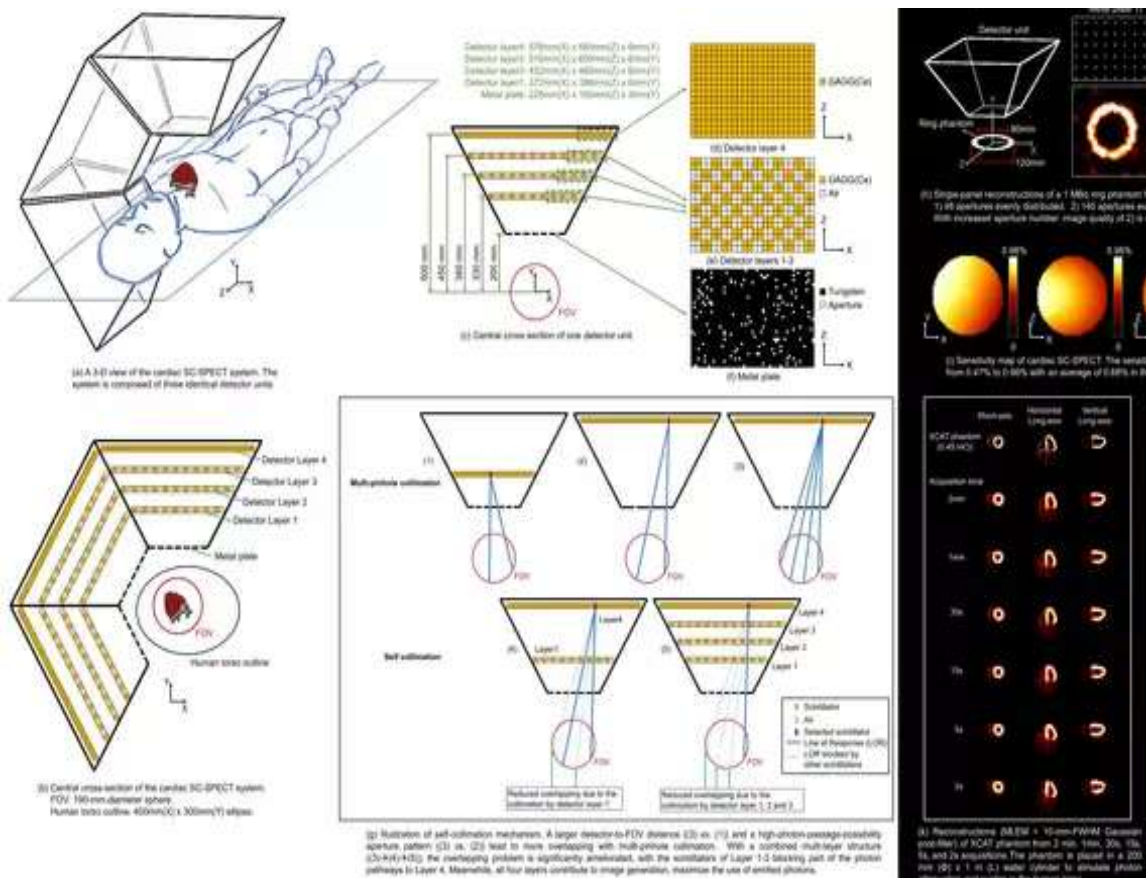
# Cardiac Instruments

## Single photon emission computed tomography (SPECT)

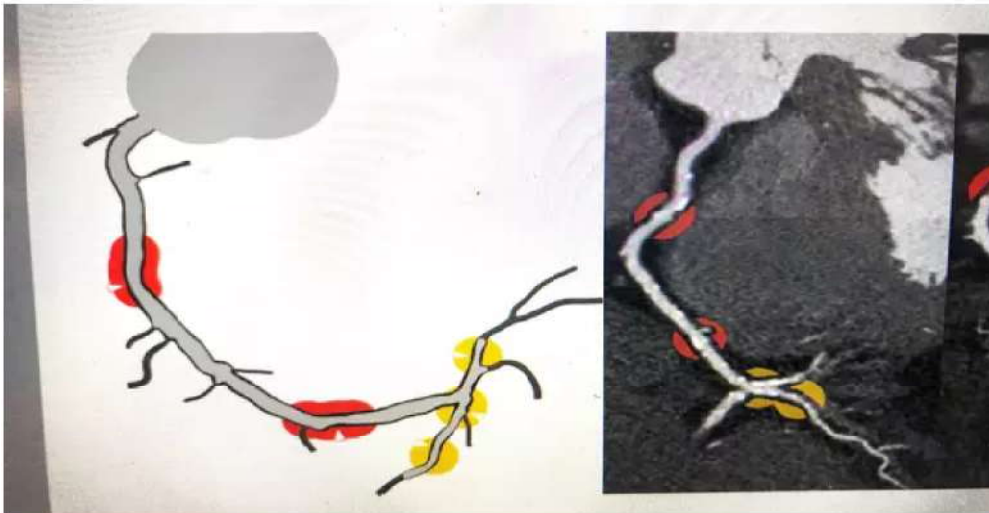
AI + cardiology

### Cardiac

### Single photon emission computed tomography (SPECT)



- ✓ Delivers images much faster than current models.
- ✓ The team presented its findings at the 2022 annual meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI)

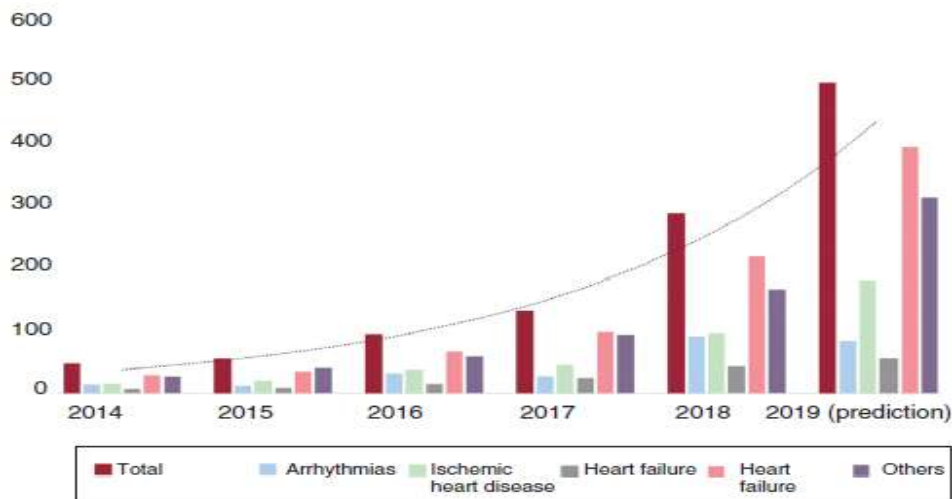


Heart-Flow's new RoadMap

Stenosis software using AI

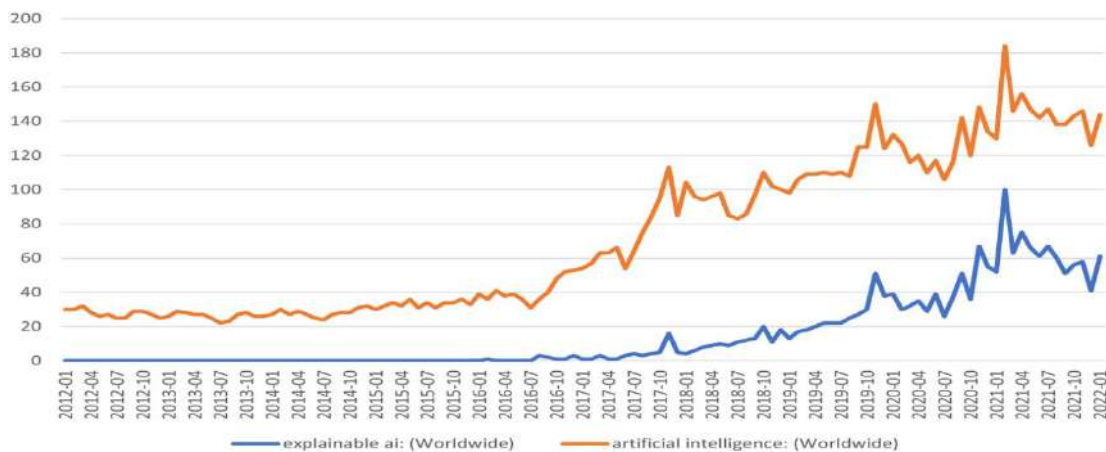
- + Shows areas of interest for possible stenting
  - o based on a patient's CT scan and FFR-CT.
- ✓ The software was rolled out commercially in April 2023

## Literature AI +cardiology

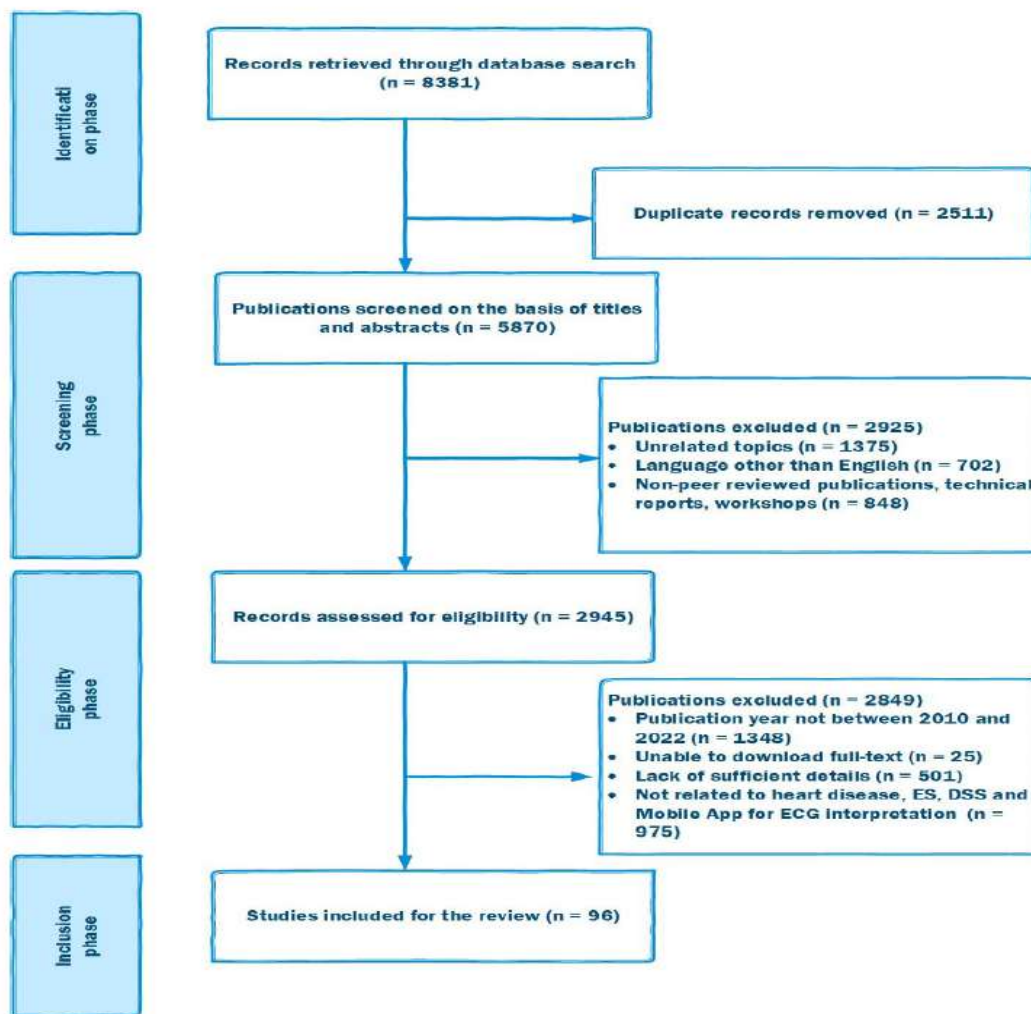


Publications indexed in PubMed

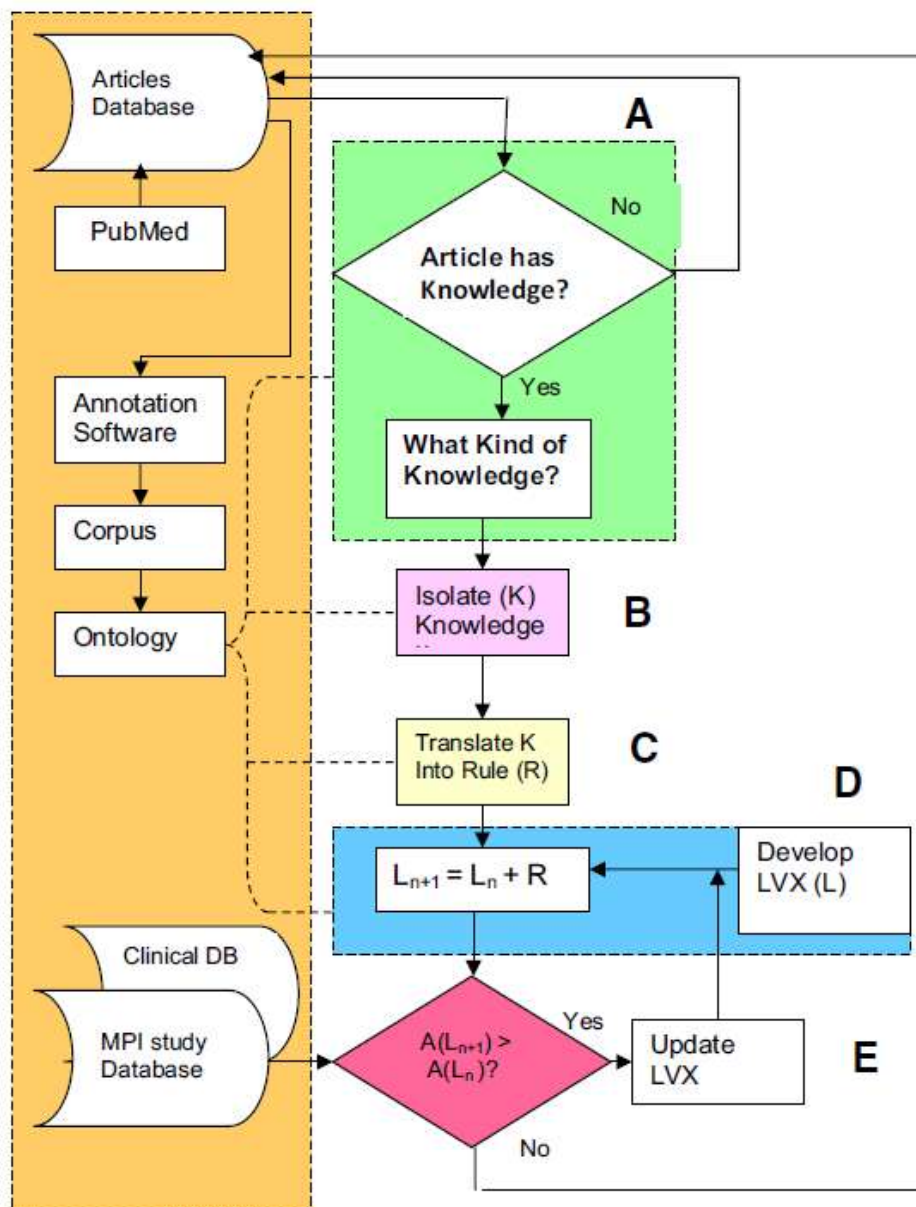
- ✓ AI, machine learning, and deep learning in cardiology.
- ✓ The details of the publications by area of interest



Google Trends is a free tool that analyzes popularity of Google search terms using real-time data. Google Trends shows trend in search terms for (AI)/explainable AI for the past 10 years. The y axis represents the normalized relative number of searches of the terms over time



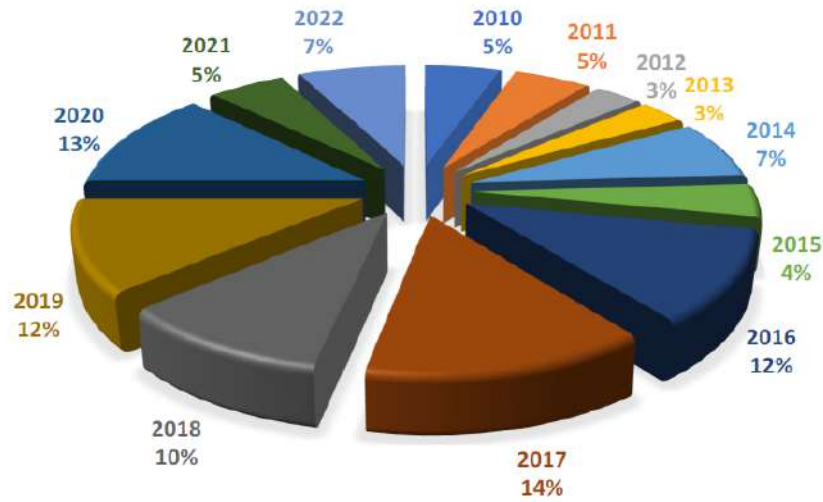
Flow chart of PRISMA model



**Process for rule learning from PUBMED articles.**

- A. Processing the articles/ abstracts selected.
- B. Automatically (or manually) isolating the text with the knowledge (K).
- C. Using the text isolated from B and automatically (or manually) translating into production rules.
- D. Taking the new production rules (R) and automatically (or manually) inserting them into the new updated expert system ( $L_n X_1$ ) called LVX.
- E. Testing LVX with MPI databases to retain rules if accuracy (A) is improved.

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Percentage distribution of the studies per year

## Applications AI +cardiology Disease prediction , Confirmation

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Area	Application	Technique	Method	Results
Arrhythmias	Prediction of paroxysmal AF from heart rate variability	Supervised learning	Data: 106 signals from 53 pairs of electrocardiograms for training Algorithms: KNN, SVM, NN	Sensitivity (100%), specificity (95%), accuracy (98%)
Arrhythmias	Prediction of AF recurrence after pulmonary vein cryoablation	Supervised learning	Data: 118 patients with 56 clinical, laboratory, and procedural variables from each patient Algorithms: GB, SVM, oversampling	Identification of 7 predictors confirming univariate statistical analysis
Arrhythmias	Classification of cardiac arrhythmia alarms in telemetry	Supervised learning	Data: PhysioNet/Computing in Cardiology Challenge 2015 Algorithm: RF	True positive, 95%; False positive, 83%
Arrhythmias	Prediction of hospital mortality in patients with resuscitated cardiac arrest from a registry	Supervised learning	Data: ANZICS registry, 39 566 patients Algorithms: LR, GB, SVM, NN, RF, combination (RF, SVM, GM)	Area under the curve of the best algorithm: 0.87 (vs 0.80 from the APACHE III scale and 0.81 from the ANZROD)
Arrhythmias	Detection of up to 17 types of arrhythmias from ECG	Supervised learning	Data: 1000 ECG signal fragments from the MIT-BIH Arrhythmia database Algorithm: convolutional NN	Accuracy (91%)
Cardiovascular risk	Prediction of cardiovascular events at 10 years from electronic medical records	Supervised learning	Data: 378 256 individuals; demographic data, medical records, medical prescriptions, and biological tests Algorithms: RF, LR, GB, NN	Area under the curve of the best algorithm: 0.76 (vs 0.72 from the ACC/AHA risk prediction scales)
Ischemic heart disease	Prediction of major cardiac adverse events in patients with acute coronary syndrome from electronic medical records	Supervised learning	Data: 2930 patients and 268 variables Algorithms: SVM and RF together with subsampling and oversampling techniques	Area under the curve of the best algorithm: 0.672 (significant improvement vs the GRACE scale, + 4.8%)

Example Algorithm Class	Advantages	Disadvantages	Example Application (Ref. #)
<b>Supervised Learning</b> Goals: Prediction of outcome, classification of observation, estimation of a parameter			
Regularized regression	Straightforward and automatic solution to high-dimensional problems Familiar interpretations for relationship of variables to outcomes	For groups of correlated features, arbitrary selection of single feature (LASSO)	Construction of a predictive model for acute myocardial infarction by using proteomic measurements and clinical variables (18)
Ensembles of decision trees	Often best "off-the-shelf" algorithm for prediction or classification Feature selection and variable importance assessment are built in	More useful for prediction than for descriptive analysis of dataset and variables Tendency to overfit data	Prediction of cardiovascular event risk (19)
Support vector machines	Transforms linear classifiers into nonlinear classifiers with the "kernel trick" Often makes highly accurate predictions	Performs nonprobabilistic classification by default Computation can be difficult in high-dimensional space	Prediction of in-stent restenosis from plasma metabolites (22)
<b>Unsupervised Learning</b> Goals: Discovery of hidden structure in a data, exploration of relationships between variables. Features discovered by unsupervised learning can often be incorporated into supervised learning models			
Deep learning algorithms	Current state-of-the-art method for feature engineering; features are often used as input for supervised learning model Wide interest across industry and academia; rapidly developing software ecosystems	Computationally expensive to train Requires a large dataset to train the model Model interpretability can be difficult	Construction of predictive representations of patients in an unsupervised fashion from electronic health records (36)
Tensor factorization	Natural incorporation of multimodal and multidimensional data	Modest number of applications thus far in published cardiovascular reports Choice of factorization algorithm is crucial for results	Subtyping of congestive heart failure with preserved ejection fraction (34)
Topological data analysis	Interpretable clustering and discovery of variable relationships	Software ecosystem less mature than for other methods Commercial offerings require licensing agreement	Subtyping of type 2 diabetes mellitus from electronic medical records (35)

- 🔔 Deep learning is included as an unsupervised learning method; however, many of the most notable applications of deep learning are those that use features learned using deep neural networks as inputs to supervised learning models.
- 🔔 In fact, the final neural network layer in a deep learning model is often simply a classification layer, and in such a case deep learning models may be considered to be an example of supervised learning.
- ✓ LASSO: least absolute shrinkage and selection operator.

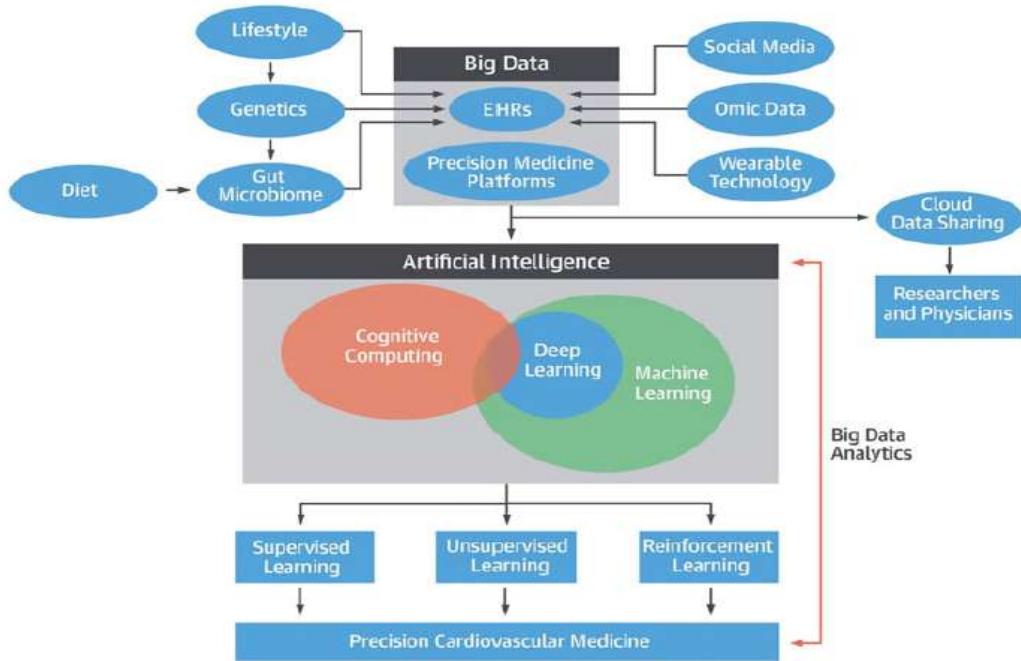
## Intervention Cardiology

## AI + cardiology

# AI +cardiology Applns

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## CENTRAL ILLUSTRATION: Artificial Intelligence in Precision Cardiovascular Medicine

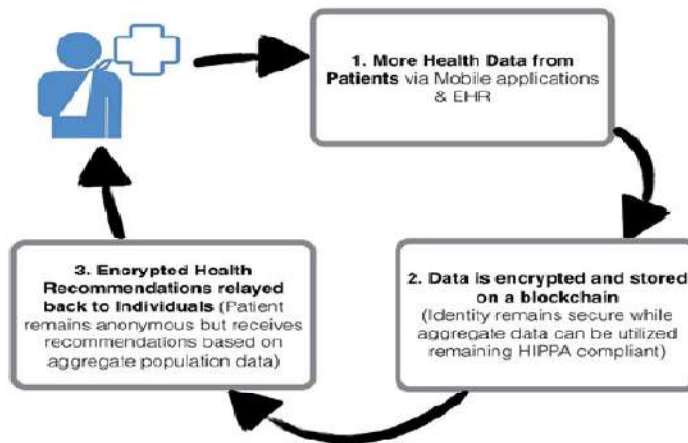


Krittanawong, C. et al. *J Am Coll Cardiol.* 2017;69(21):2657–64.

Interplay of big data, AI and precision cardiovascular medicine.

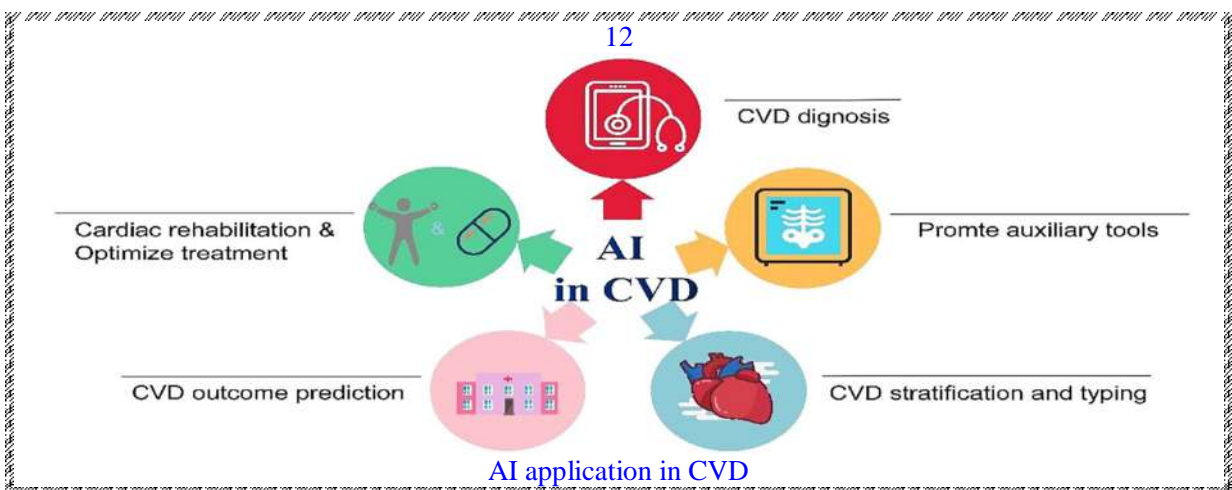
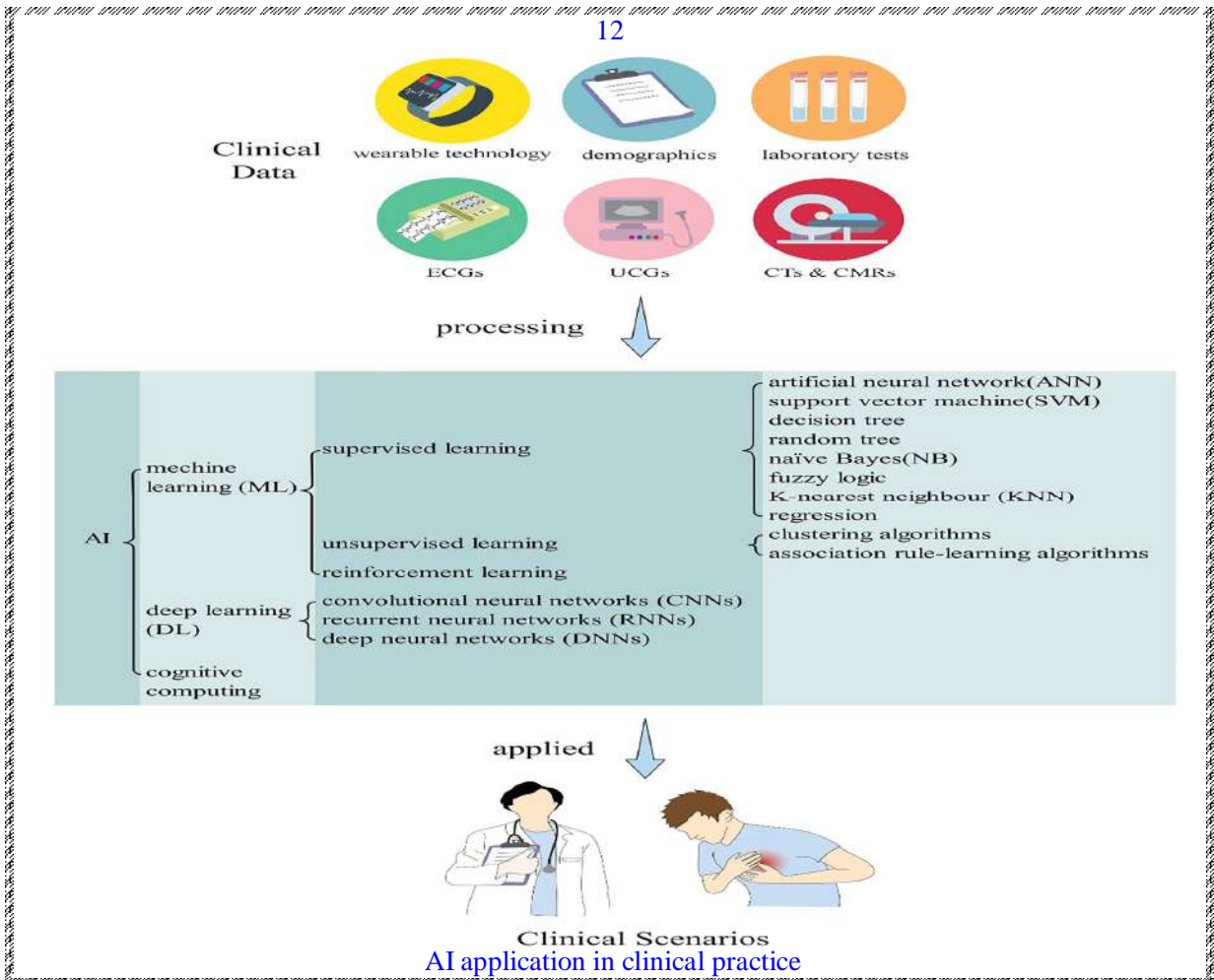
- ✓ Ref: Krittanawong C, et al. Precision cardiovascular medicine. *J AM Coll Cardiol:* 20167;69(21); 2657–64.

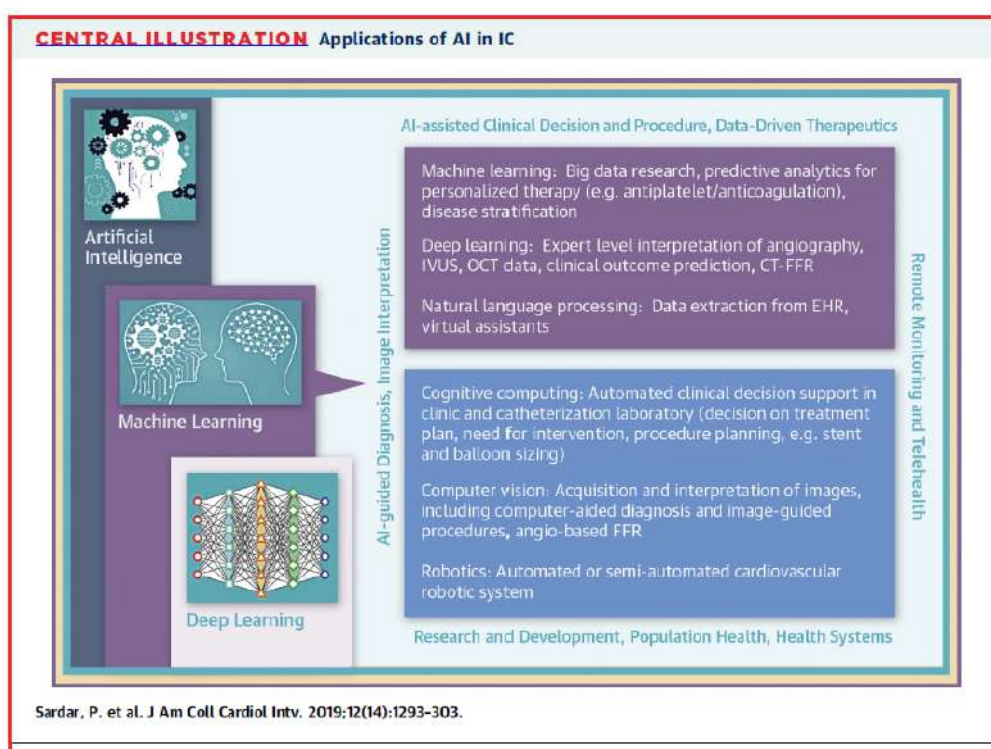
34





✓ An example of an individual patient's data can be de-identified, encrypted, and stored on the cloud to amass the volume of aggregate patient data necessary for the development artificial intelligence solutions to relay back personalized clinical inferences.





### Applications of artificial intelligence (AI)

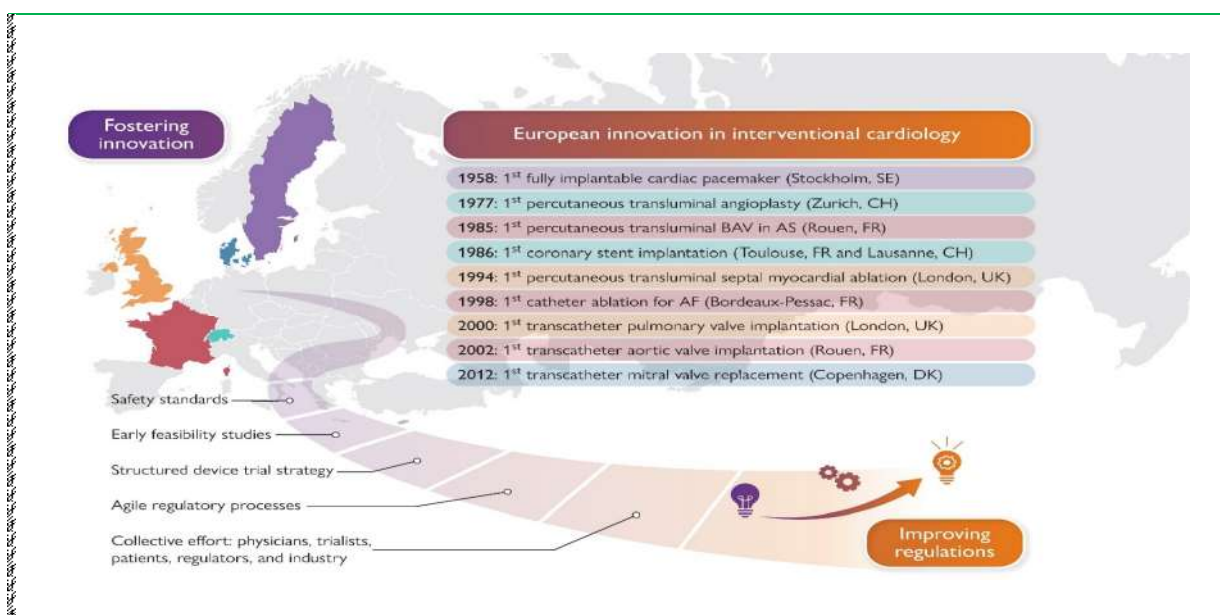
- AI-guided diagnosis, image interpretation, clinical decision support, data driven therapeutics, research and development, population health, efficient administration, workflow and regulation, and AI-assisted interventional procedures.

EHR : electronic health record;

CT-FFR : computed tomography fractional flow reserve;

IVUS : intravascular ultrasound;

OCT: optical coherence tomography

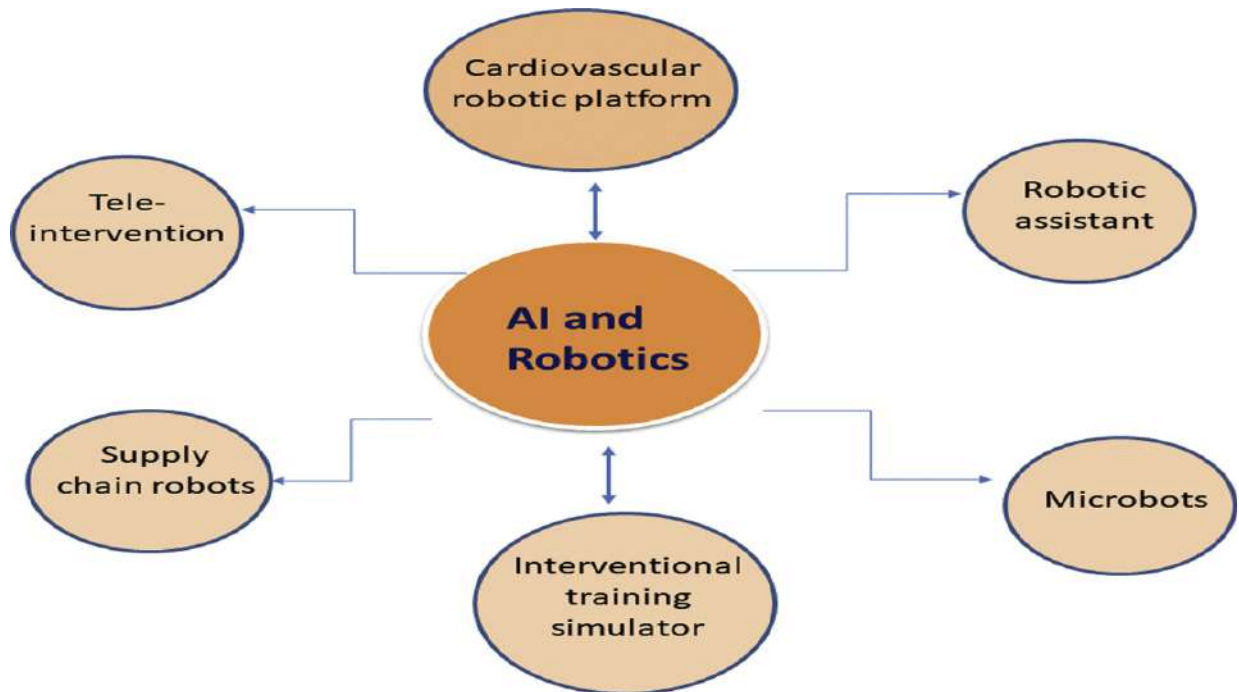


**FIGURE 5** Advantages and Challenges of AI in IC

Advantages and challenges of Artificial Intelligence in Interventional Cardiology	
Advantages	Challenges
Precision, accuracy and data driven decisions on diagnosis and treatments	Complexity and Cost
Procedural assistance	Lack of human touch, common sense
Integration of large and diverse information	Concerns regarding privacy and security, "black box" design
Decrease Inter-observer and intra-observer variability	Lack of large well curated clinical or imaging data or "Training dataset"
Better in repetitive, laborious, time-consuming job	Regulation, legal and liability issues
Time saving administrative process, cath lab workflow	Threat to human job

46

Applications of Robotics in IC



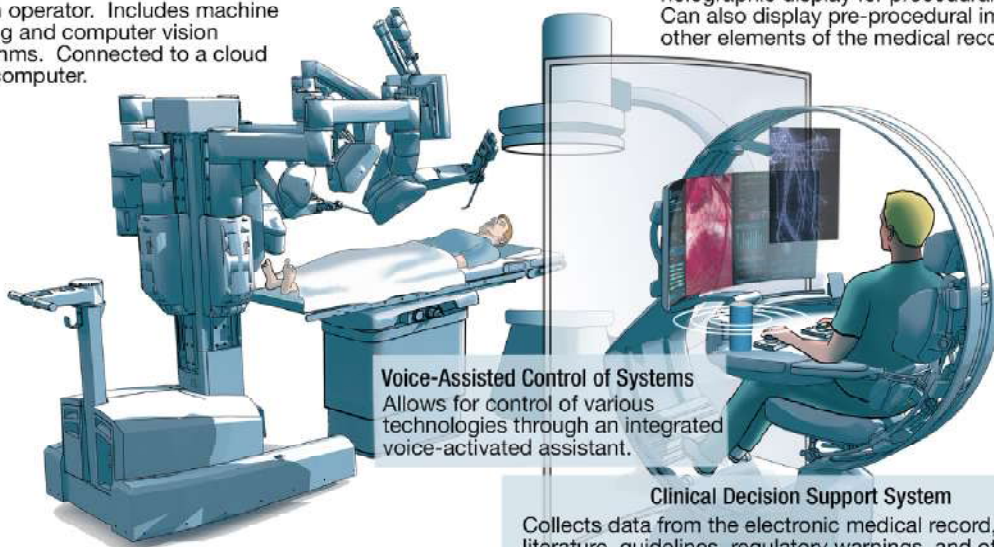
# Future Perspective AI +cardiology

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## Future Catheterization Laboratory With Artificial Intelligence-Enabled Technologies

### Semi-autonomous Vascular Robotic System

Performs many procedural steps with minimal assistance from a remote human operator. Includes machine learning and computer vision algorithms. Connected to a cloud supercomputer.



### Augmented Reality System

Real-time viewing, measurement, and manipulation of patient anatomy in a holographic display for procedural guidance. Can also display pre-procedural images and other elements of the medical record.

### Voice-Assisted Control of Systems

Allows for control of various technologies through an integrated voice-activated assistant.

### Clinical Decision Support System

Collects data from the electronic medical record, medical literature, guidelines, regulatory warnings, and other internet-based public information. Provides analysis of intra-procedural progress that integrates this data with procedural imaging and patient status. Includes predictive analytics with the use of cognitive computing to support optimal clinical decision making.

## Artificial intelligence-enabled future catheterization laboratory with

- ! Clinical decision support system,
- ! Voice-powered virtual assistant,
- ! Augmented reality platforms, and
- ! Semiautonomous/  
! Autonomous robotic system

# VR, AR, Mixed Reality AI +cardiology

46

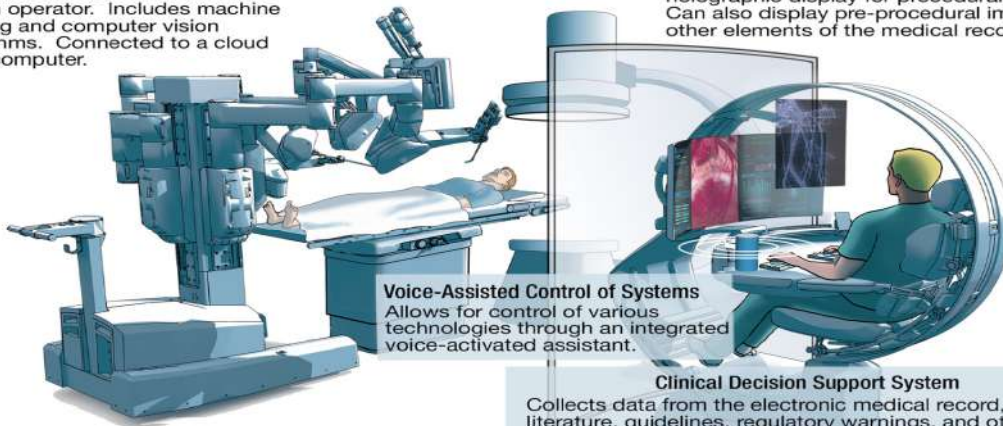
## Augmented Reality Cardiac Holographic Display for Procedural Guidance



49

**Semi-autonomous Vascular Robotic System**  
Performs many procedural steps with minimal assistance from a remote human operator. Includes machine learning and computer vision algorithms. Connected to a cloud supercomputer.

**Augmented Reality System**  
Real-time viewing, measurement, and manipulation of patient anatomy in a holographic display for procedural guidance. Can also display pre-procedural images and other elements of the medical record.



**Voice-Assisted Control of Systems**  
Allows for control of various technologies through an integrated voice-activated assistant.

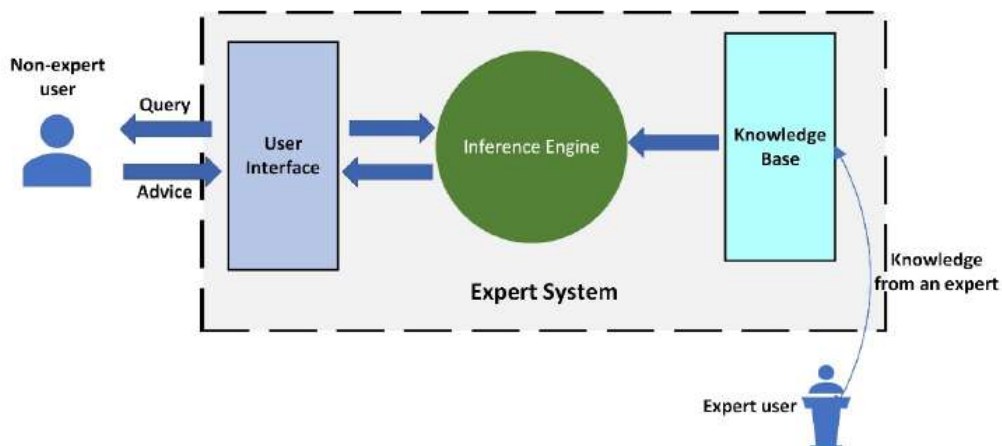
**Clinical Decision Support System**  
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### AI-enabled future catheterization laboratory

- 🔔 Clinical decision support system,
- 🔔 Voice-powered virtual assistant,
- 🔔 Augmented reality platforms,
- 🔔 Semiautonomous/autonomous robotic system

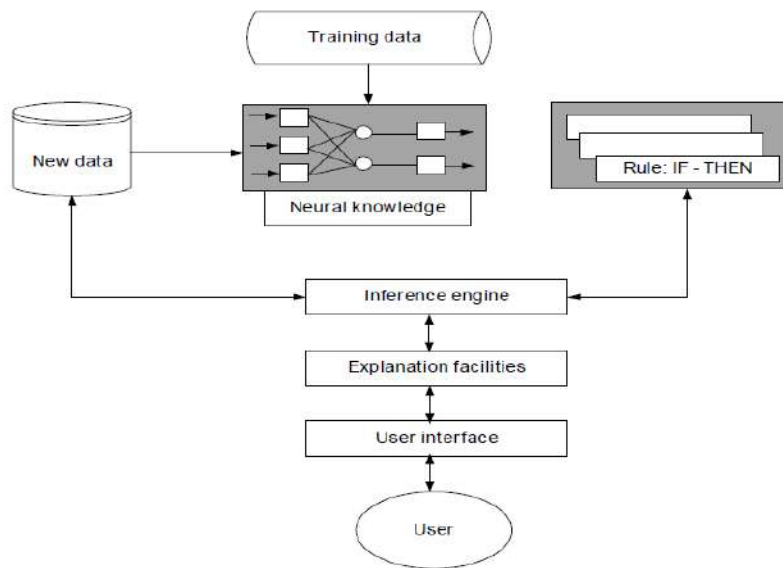
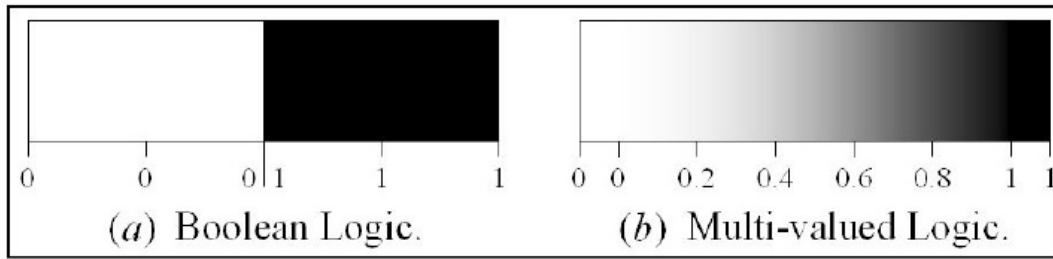


## Expert systems (ES) Fuzzy logic

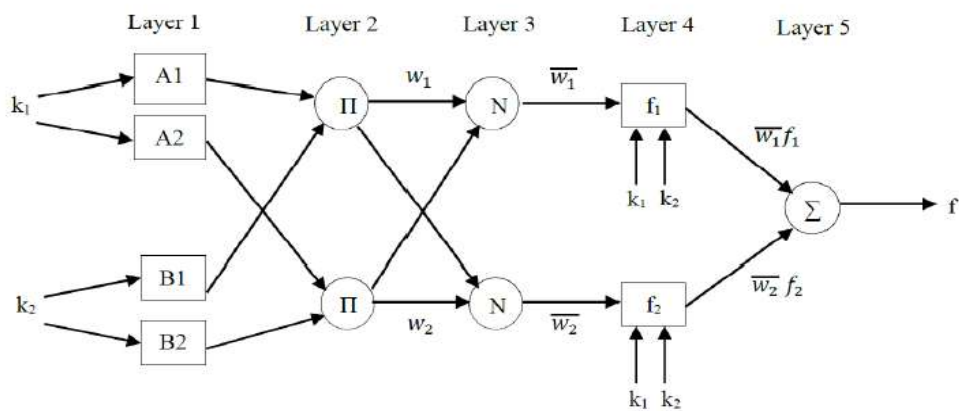


Components or structure of an expert system

## Range of logical values in Boolean and fuzzy logic



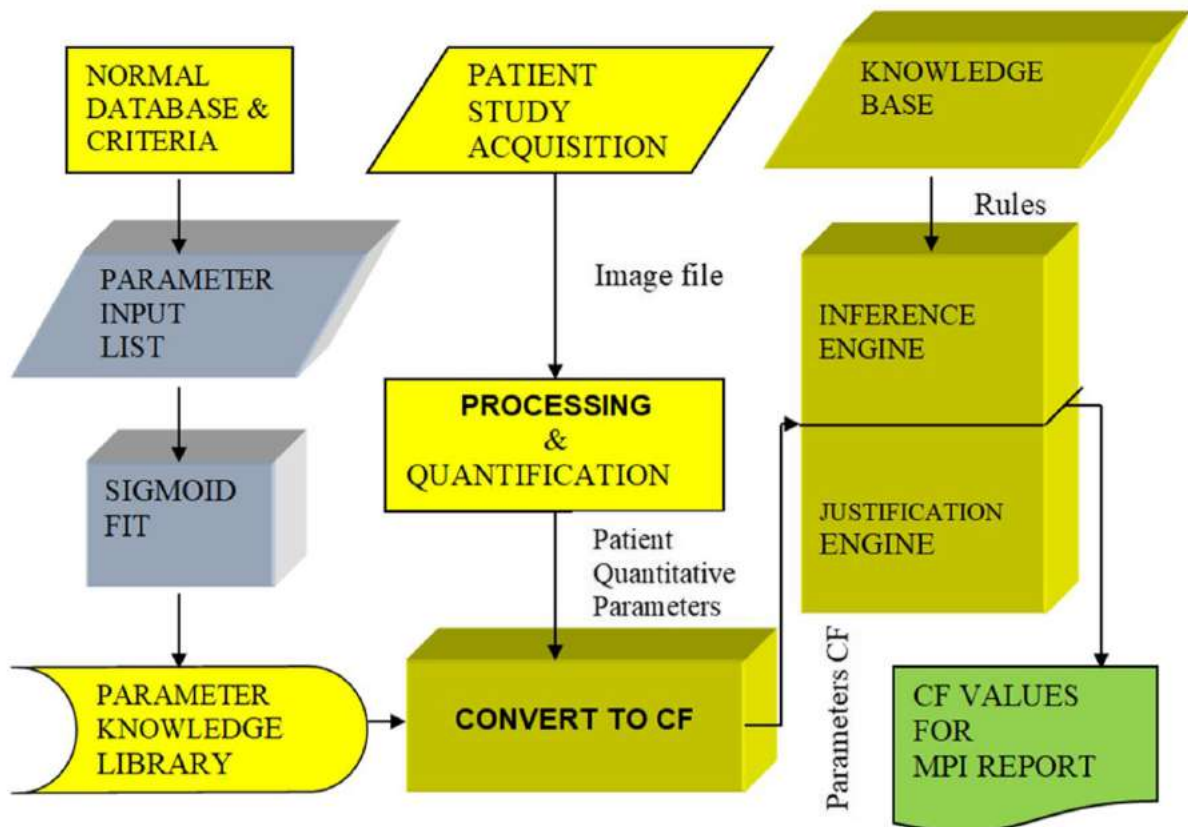
Basic structure of a **neural expert system**



The architecture of a **neuro-fuzzy inference system**

# LV Expert systems (LVX) Fuzzy logic

38



Flow diagram for LVX Expert System.

- ✓ This diagram shows the flow of how a patient's MPI study is acquired, processed, and quantified
  - ? to extract perfusion, function, and viability parameters.
  - ? These parameters are converted to certainty factors (CF).
  - ? Then the input to the LV expert system (LVX).
- ✓ The expert system is comprised of
  - ! knowledge base, the inference engine and the justification engine.
  - ! The trapezoidal blocks indicate domain expert knowledge;
  - ! the rectangular blocks indicate software algorithms.
  - ! The parameter knowledge library is only generated once and then regenerated only when the knowledge that creates the parameter input list is enhanced by more experience or more data.



Annotation Results for 7769451.txt.xml in processed

Click In Text to See Annotation Detail

Annotations

- Ontology ("SPECT")
  - begin = 1812
  - end = 1817
- MerlinAcronym
  - MerlinAcronym ("SPECT")
    - begin = 1812
    - end = 1817
    - expandedForm = single photon en
- Conclusion
  - Conclusion ("Gating provides a valuabl")
    - begin = 1758
    - end = 1893

Legend

Conclusion  DocumentAn...  MerlinAcronym  Ontology

Select All Deselect All Hide Unselected

### Document annotation viewer and analyzer.

- ! Output of an Annotation Viewer and Document Analyzer using IBM's Unstructured Information Management Architecture
  - o to facilitate the human experts visualize the information from a pertinent abstract and manually compare the results of the automated knowledge ranking.
- ! The different sections of the abstracts are automatically identified and annotated using the ontology terms for the nuclear cardiology domain

### Integrating artificial intelligence and natural language processing

```

P1:   RC1 RA1 → OUT1
RC1:  [CONF] LV_artifact
LV_stress_perfusion_is_abnormal
RA1:  HAS (PATIENT, ([GENDER], DEFECT))
LV_artifact))
      HAS (PATIENT, FUNCTION)
OUT1: IF GENDER AND DEFECT AND FUNCTION
      THEN CONF LV_artifact
      LV_stress_perfusion_is_abnormal

DEFECT: [NOT] LV_perfusion_defect_is_reversible( POSITION )
FUNCTION: [NOT] LV_resting_function_is_abnormal
GENDER:  (Gender_is(male) | Gender_is(female))
POSITION: (inferior|anterior)

P2:   RC2 RA2 → OUT2
RC2:  [CONF]_[NOT]
RA2:  HAS (PATIENT, (DEFECT, FUNCTION,
OUT2: IF LV_artifact AND DEFECT AND
      THEN CONF
  
```

**A : Example rule extraction pattern**

```

Applying Pattern P1 generates two rules, R1 and R2:
R1:  IF Gender_is(female) AND NOT
      LV_perfusion_defect_is_reversible(anterior)
      AND NOT LV_resting_function_is_abnormal
      THEN STRONG_EVIDENCE LV_artifact

R2:  IF Gender_is(male) AND
      NOT LV_perfusion_defect_is_reversible(inferior) AND
      NOT LV_resting_function_is_abnormal
      THEN STRONG_EVIDENCE LV_artifact

Applying Pattern P2, using the output of Pattern P1, to generate rule R3:
R3:  IF LV_artifact AND NOT LV_perfusion_defect_is_reversible AND
      NOT LV_resting_function_is_abnormal
      THEN STRONG_EVIDENCE NOT LV_stress_perfusion_is_abnormal
  
```

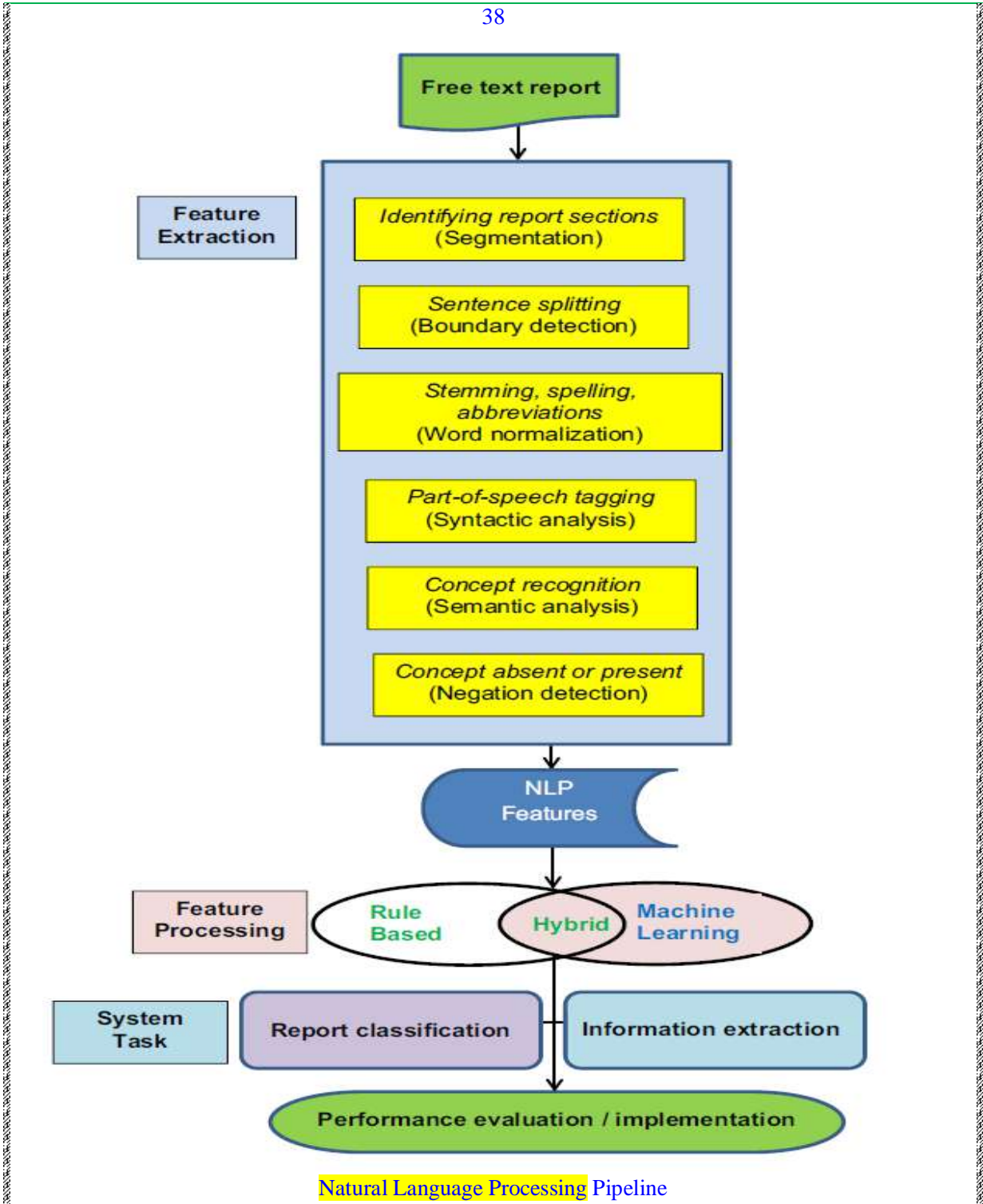
**B: Production rules generated using rule patterns in A.**

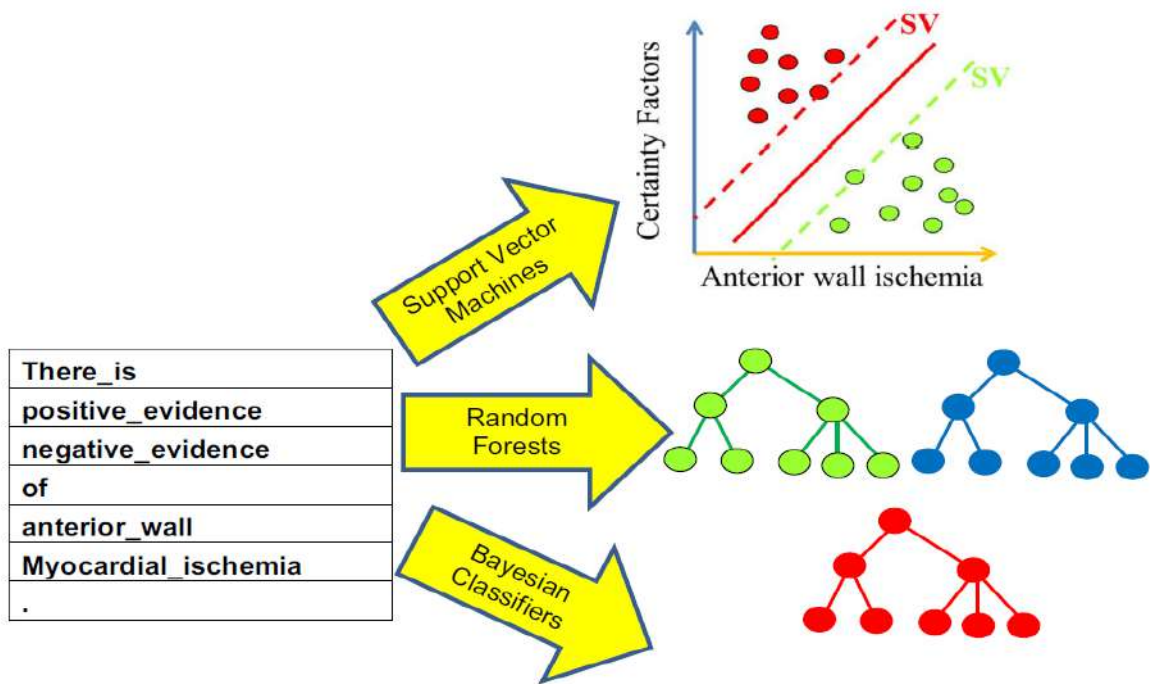
### Pattern development for production rules extraction.

- A. Example of two rule patterns, P1 and P2, developed. The antecedent of pattern P1 requires the text to specify the patient's gender, the type of defect (e.g., fixed defect), and heart function (e.g., "normal systolic function"). If matched, the system stores the variable bindings for reuse of other patterns, and outputs a production rule.
- B. When Pattern P1 is applied to a semantic network; it generated the resulting assertions (Rule 1 and Rule 2). Then, pattern P2 is applied, using values extracted by pattern P1, resulting in Rule 3.

# Natural Language Processing (NLP)

38

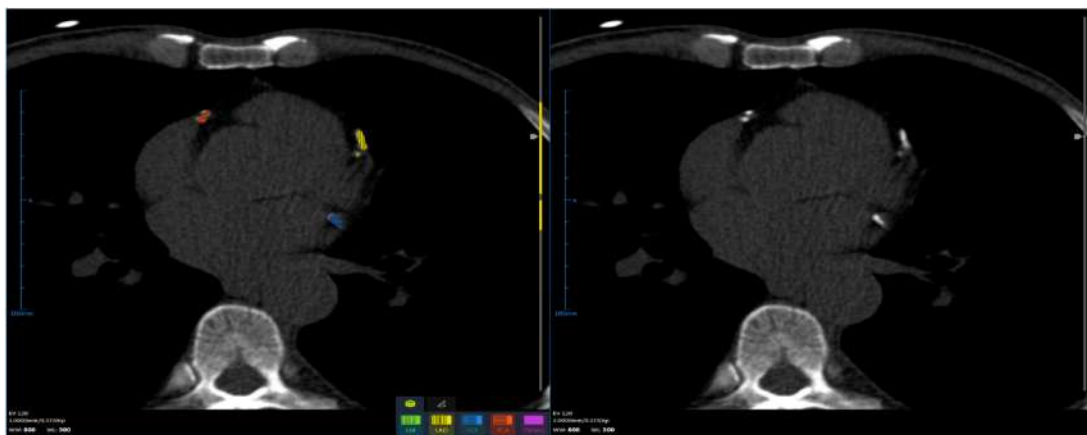




Classic machine learning NLP techniques.

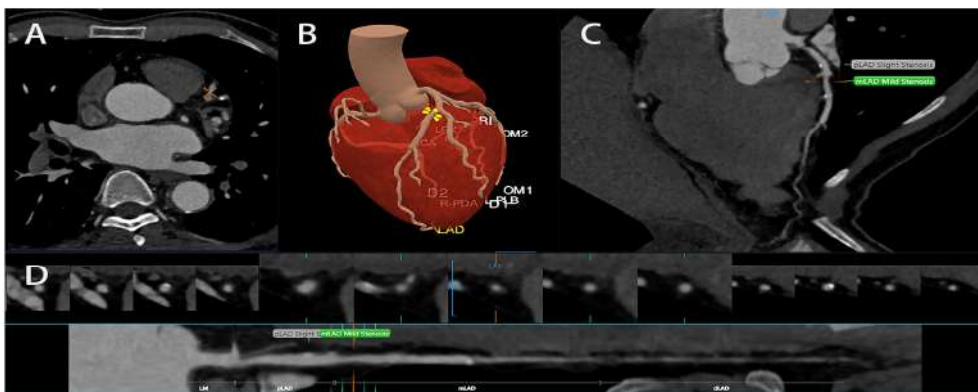
- ✓ Support vector machines, random forests, and Bayesian systems use vector representations of text for classification task.

# Stenosis



Coronary artery calcification

🔔 Identification, segmentation, and scoring Using AI

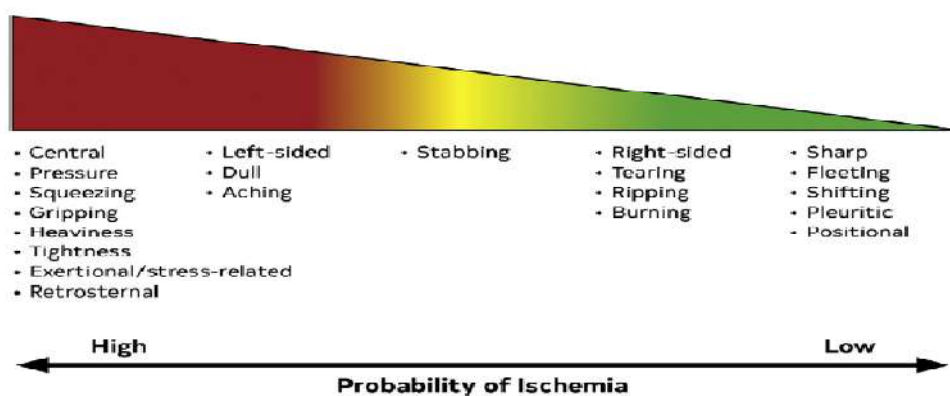


- ✓ AI-Coronary arteries (A)
- ✓ Segments them (B)
- ✓ Identifies and classifies coronary plaques, and measures the severity of stenosis (C,D).

### Diagnostic performance of artificial intelligence in coronary stenosis

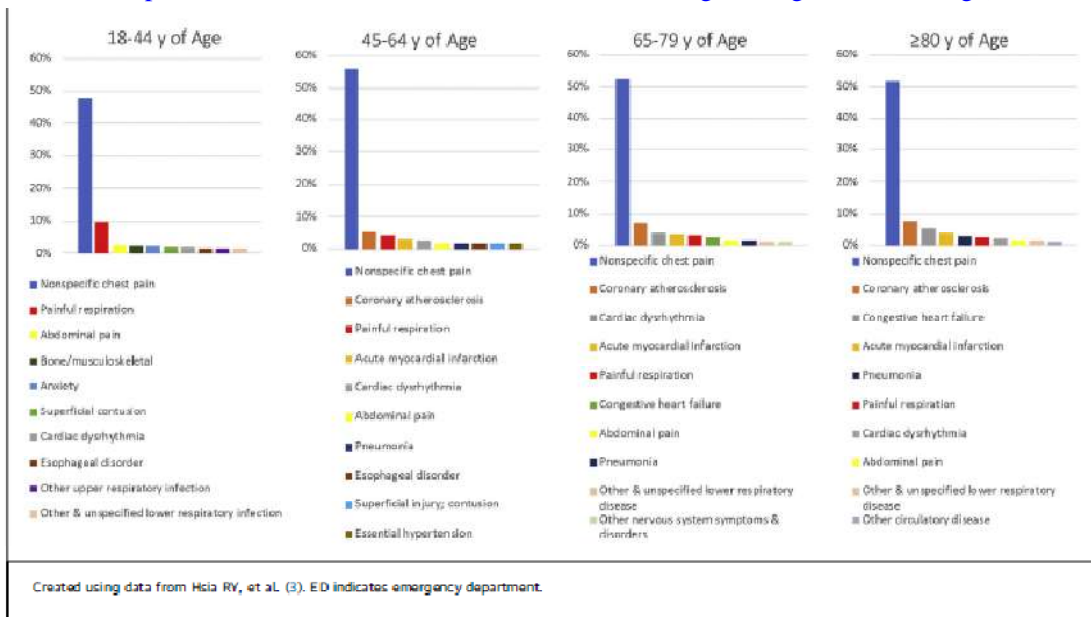
Year	Methods	Sensitivity	specificity	PPV	NPV	Accuracy
2015	SVM	93%	95%	NA	NA	94%
2020	DL	94%	63%	94%	59%	NA
2010	Computer-aided	100%	65%	58%	100%	100%
2011	Supervised Learning	97.62%	67.14%	NA	99.77%	NA
2012	CAST	>90%	40%–70%	NA	> 95%	NA

- ✓ DL, deep learning; SVM, support vector machine; PPV, positive predictive value;
- ✓ NPV, negative predictive value; NA, not applicable
- ✓ CAD, coronary artery disease;
- ✓ QCA, quantitative coronary angiography; CCTA, coronary CT angiography;
- ✓ CAST, computer-aided simple triage;

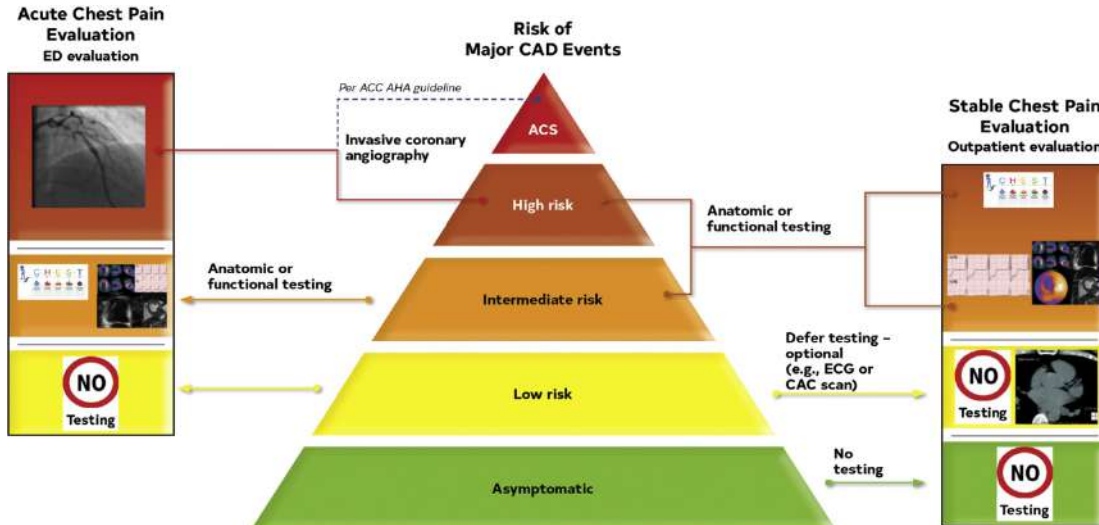


Index of Suspicion That Chest "Pain" Is Ischemic in Origin on the Basis of Commonly Used Descriptors

Top 10 Causes of Chest Pain in the ED Based on Age (Weighted Percentage)



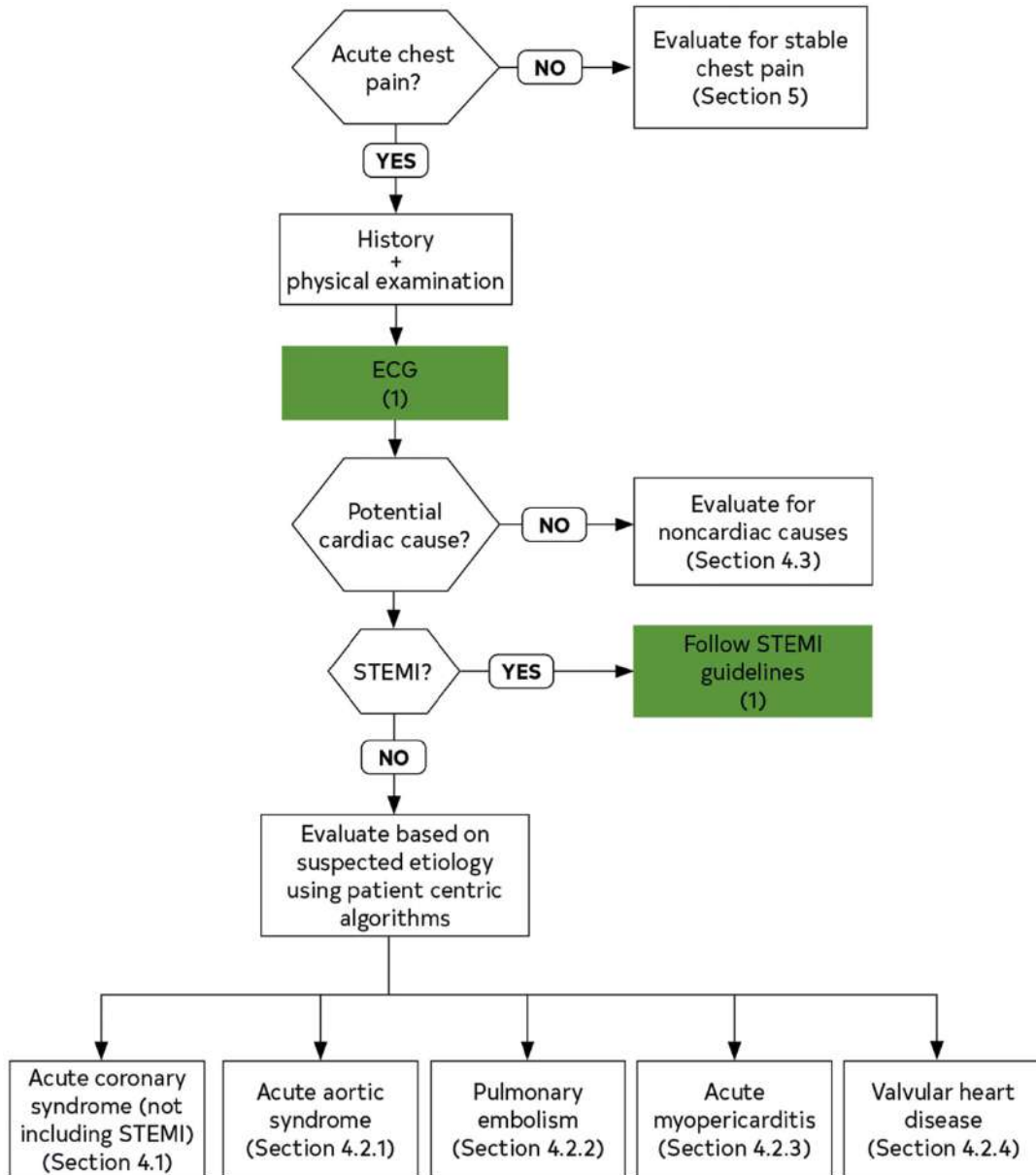
Chest Pain and Cardiac Testing Considerations



The choice of imaging depends on the clinical question of importance, to either a) ascertain the diagnosis of CAD and define coronary anatomy or b) assess ischemia severity among patients with an expected higher likelihood of ischemia with an abnormal resting ECG or those incapable of performing maximal exercise.

ACS: acute coronary syndrome; CAC, coronary artery calcium; CAD, coronary artery disease; ECG, electrocardiogram.

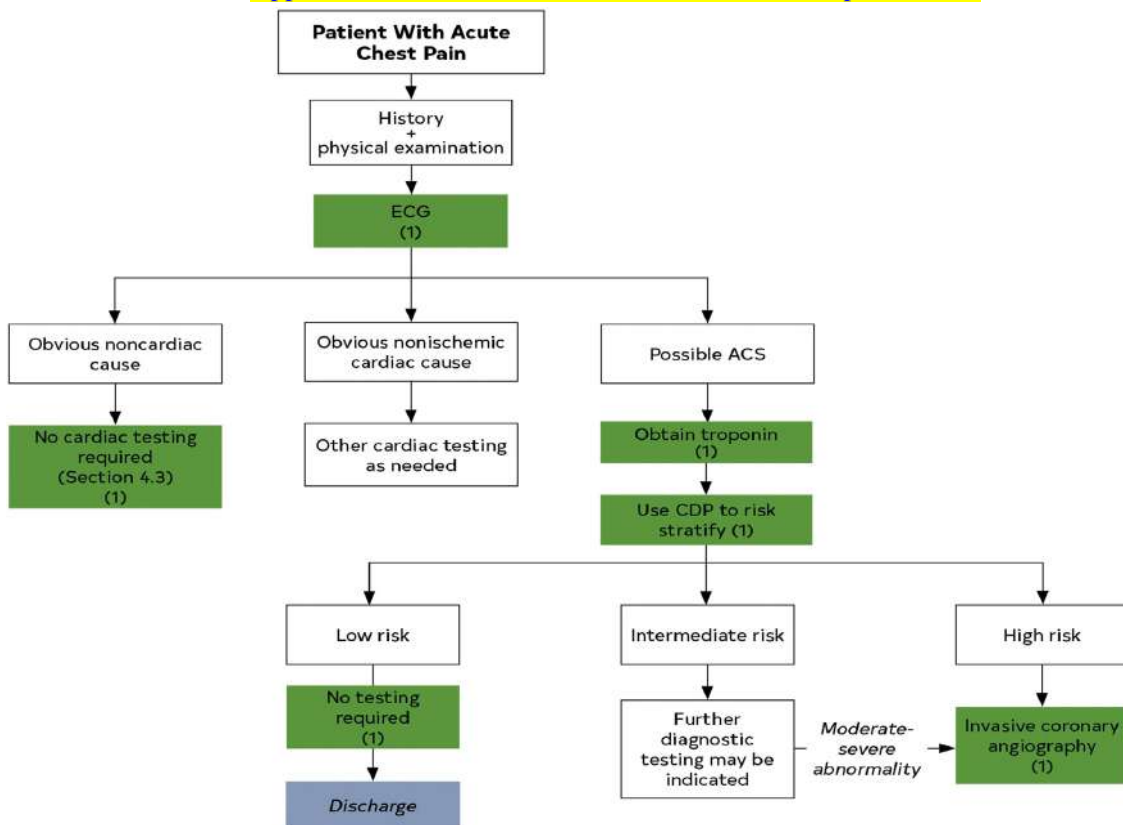
## Patient-Centric Algorithms for Acute Chest Pain



STEMI, ST-segment–elevation myocardial infarction

ECG: electrocardiogram;

General Approach to Risk Stratification of Patients with Suspected ACS



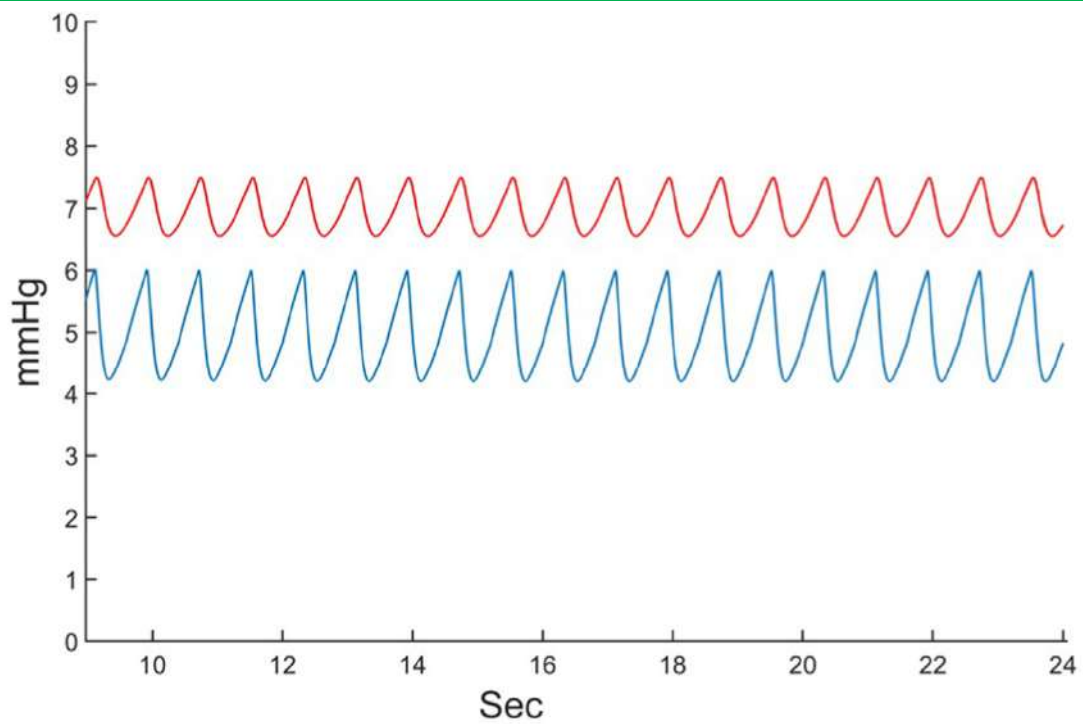
ACS: acute coronary syndrome; CDP, clinical decision pathway;

ECG



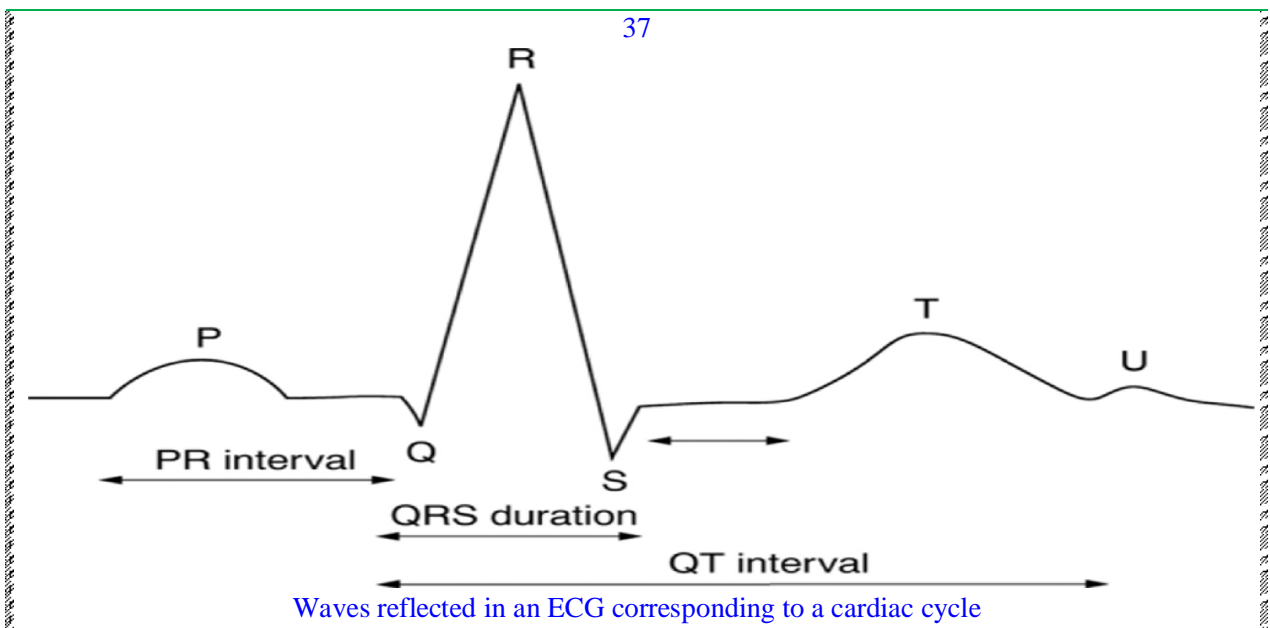
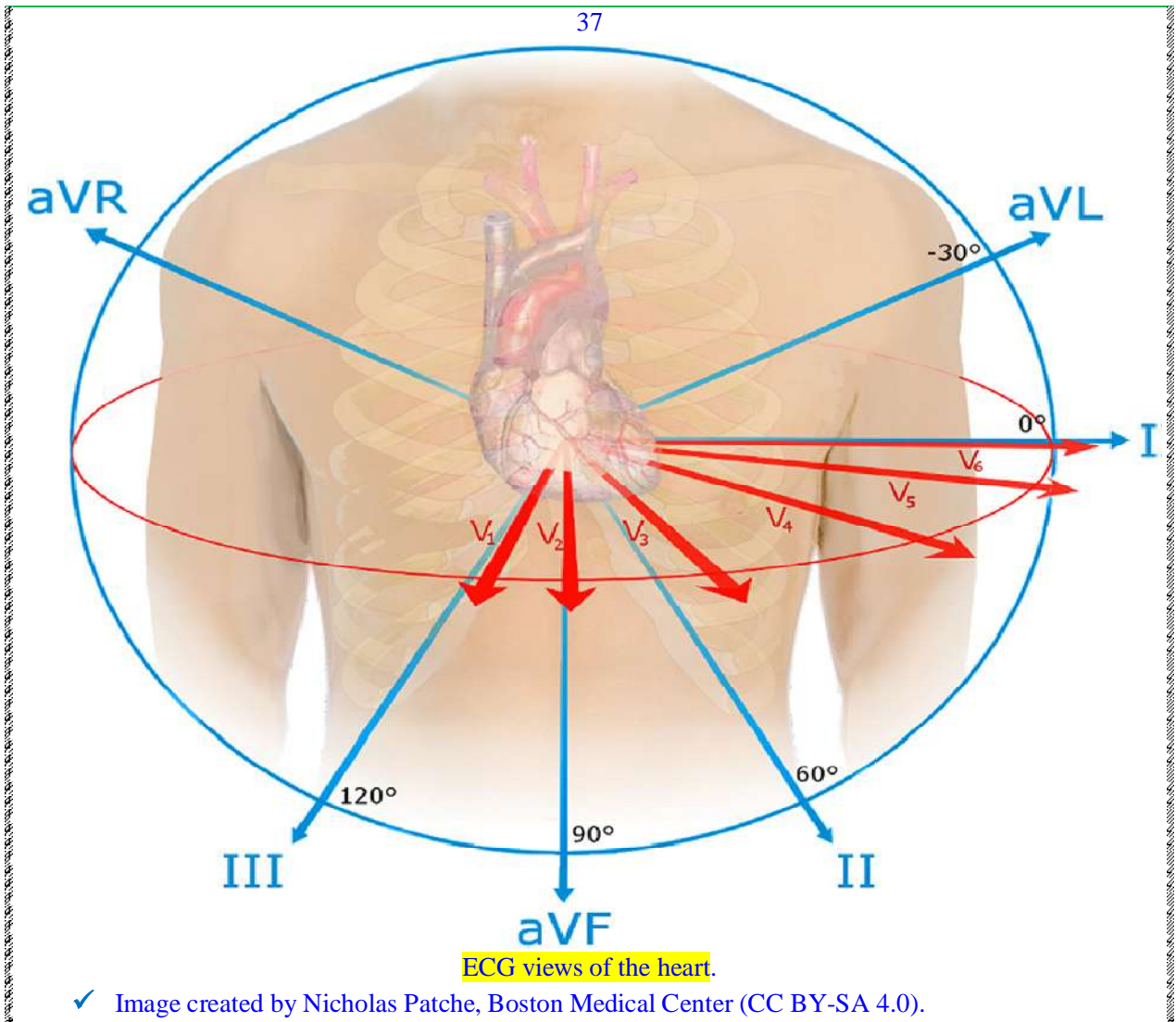
AI improves diagnosis and treatment for patients

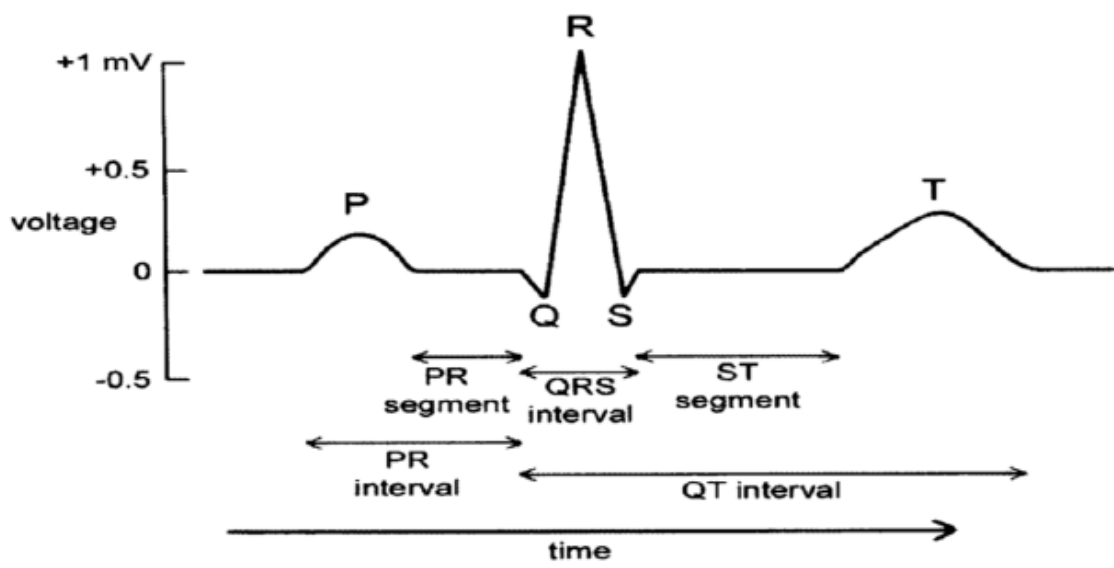
🔔 AI-enabled clinical tools have to be easily available and used



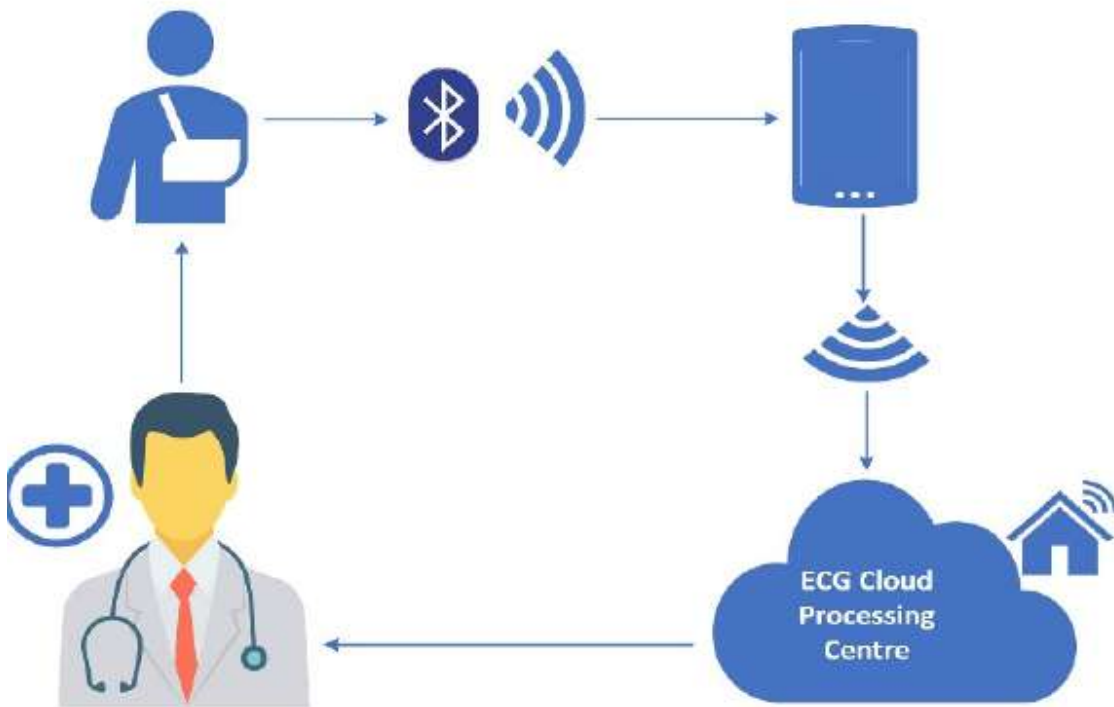
Pulsations in the pulmonary artery (top) and pulmonary veins (bottom) in computer simulations without an RV.







A typical ECG waveform for one cardiac cycle measured from the lead II position



A generic design architecture of an ECG mobile

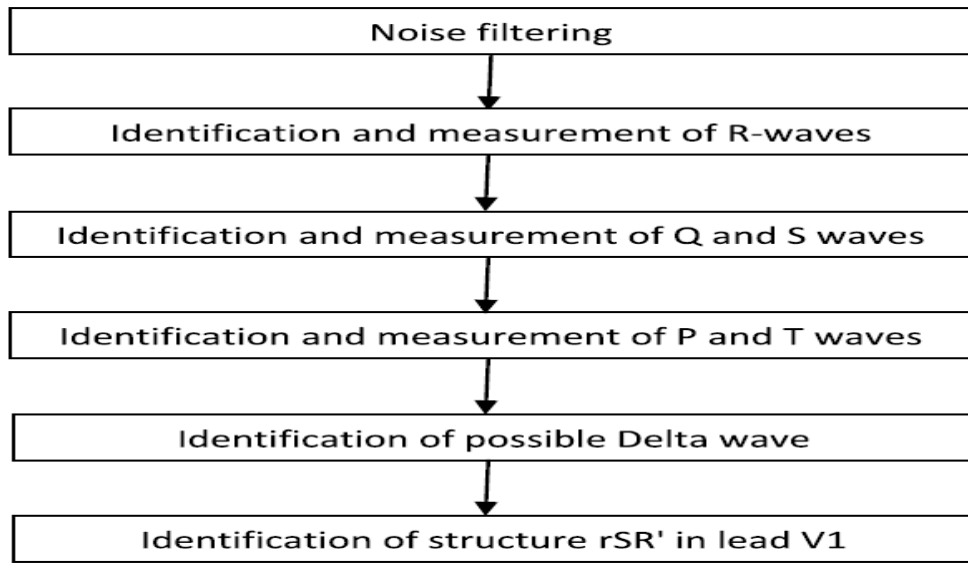
## ECG features in different cardiovascular conditions.

Cardiovascular condition	Common ECG features
Atrial Fibrillation (AF)	Absence of P-waves Irregularly irregular R-R intervals Fibrillatory waves (f-waves) instead of P-waves ST-segment depression or elevation
Myocardial Infarction (MI)	ST-segment elevation (STEMI) ST-segment depression (NSTEMI) T-wave inversion Q-waves (pathological Q-waves)
Atrial Flutter	Sawtooth-shaped flutter waves (F-waves) Regular R-R intervals (2:1, 3:1, etc.) ST-segment changes (often with rapid ventricular response)
Ventricular Tachycardia (VT)	Wide QRS complexes (>0.12 s) Absence of P-waves before QRS complexes Regular or irregular rhythm
Ventricular Fibrillation (VF)	Chaotic and irregular QRS complexes Absent P-waves and T-waves “Quivering” appearance of the ECG trace

## Set of 15 diagnoses and number of cases in the database.

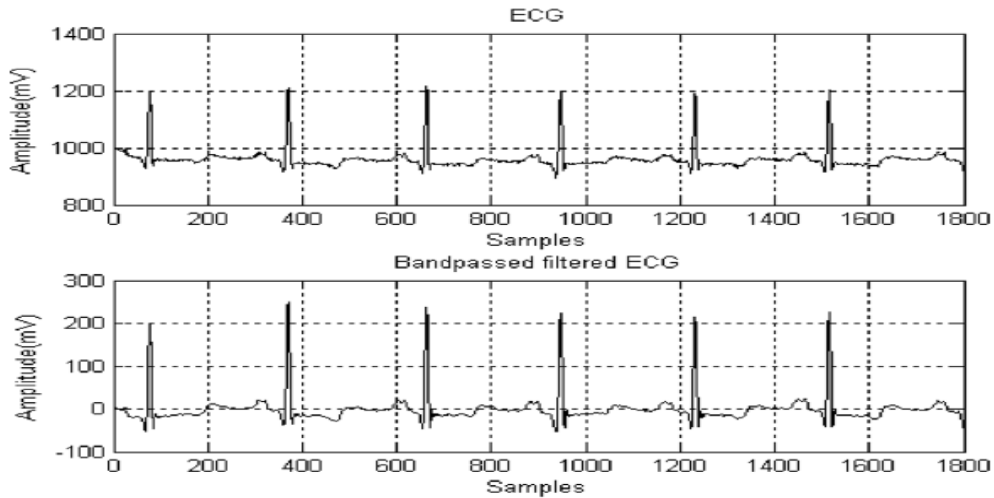
Diagnosis	Number of cases
Normal	212069
Artifactual or bad performance	1138
Incomplete right branch block	26375
Complete right branch block	2407
Incomplete right branch block with narrow QRS	Not registered
1st degree atrioventricular block	565
Wolff–Parkinson–White preexcitation	163
Complete arrhythmia due to atrial fibrillation	181
Long QT	Not registered
Short QT	Not registered
Sinus tachycardia	2248
Sinus bradycardia	21439
Nodal/ectopic atrial rhythm	Not registered
Sinus arrhythmia	Not registered
Cardiac arrhythmia	2164

37



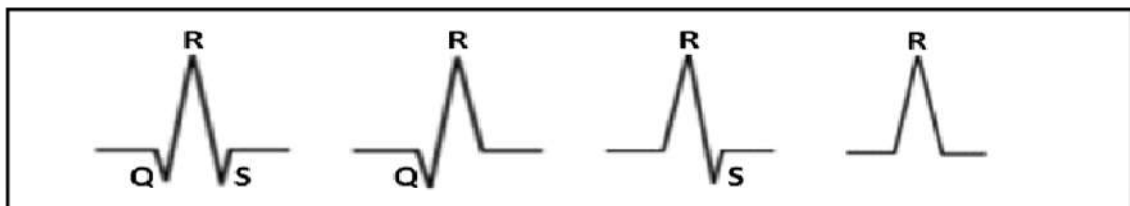
Stages for the identification and measurement of waves

37

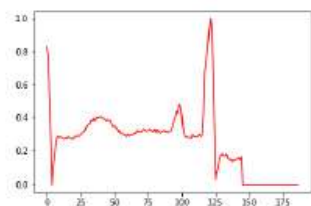


Second-order Butterworth bandpass filter in ECG (Fazel-Rezai et al., 2011)

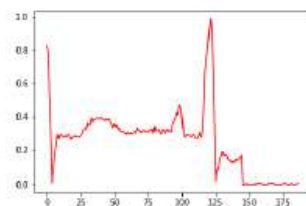
37



Possible QRS patterns to be detected

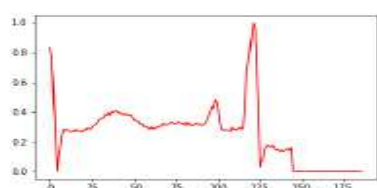


(a) classify clean ECG as "N"

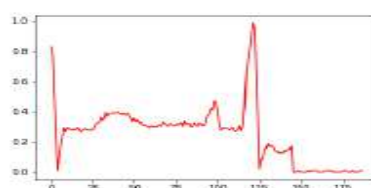


(b) classify "noisy" ECG as "V"

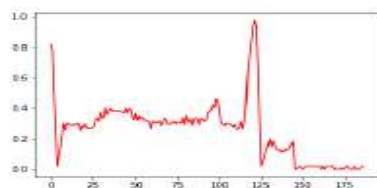
ECG single (a) was added with adversarial noise (b)



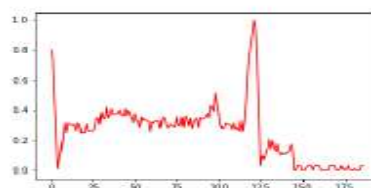
(a) clean ECG (noise level 0), classified as "N"



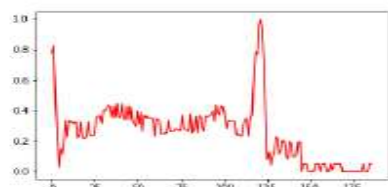
(b) ECG on noise level 0.01, classified as "V"



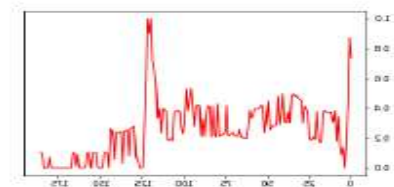
(c) ECG on noise level 0.02, classified as "V"



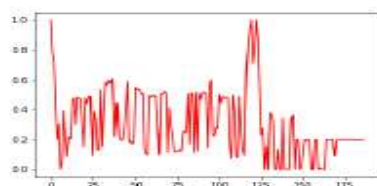
(d) ECG on noise level 0.03, classified as "V"



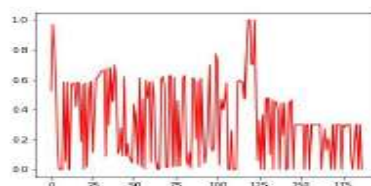
(e) ECG on noise level 0.05, classified as "V"



(f) ECG on noise level 0.1, classified as "V"



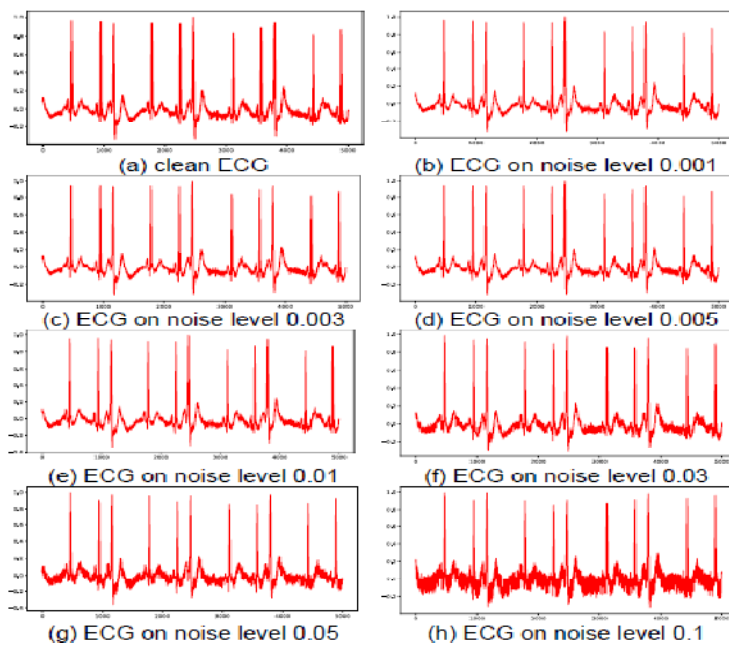
(g) ECG on noise level 0.2, classified as "S"



(h) ECG on noise level 0.3, classified as "F"

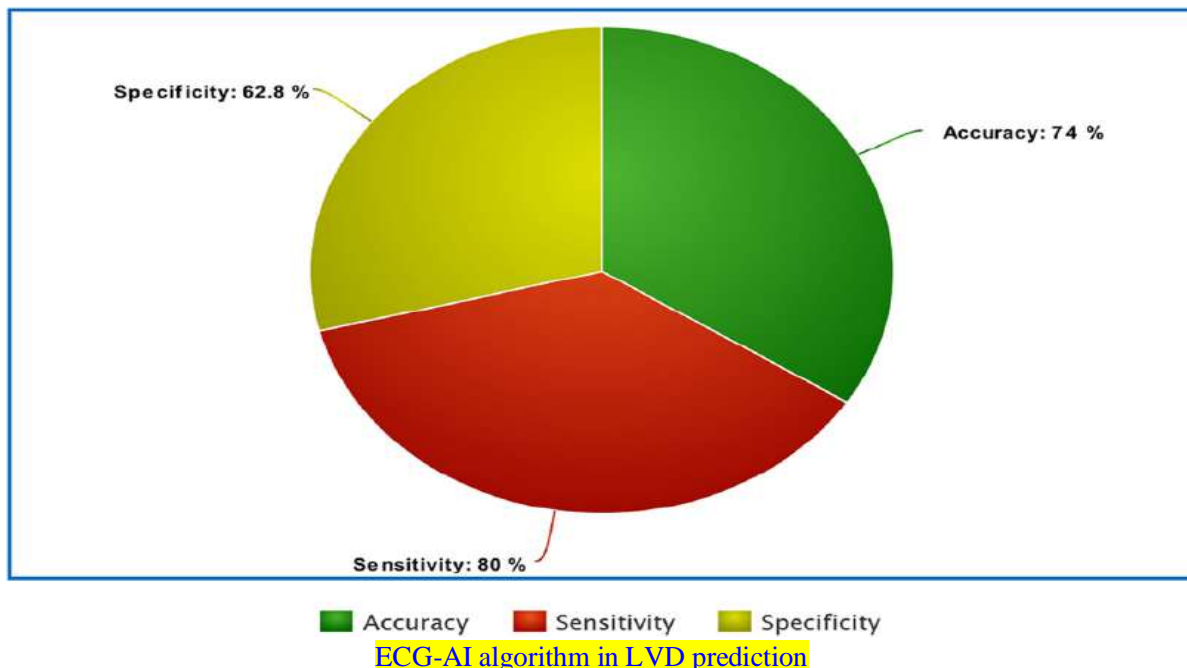
MIT-BIT ECG signals on different noise levels.

- ✓ The original classification label is N (normal).
- 🔔 When the noise level is 0.01
- 🔔 Then, MLP classified it as V (premature ventricular contraction and ventricular escape).



CPSC2018 ECG Lead I on different noise levels

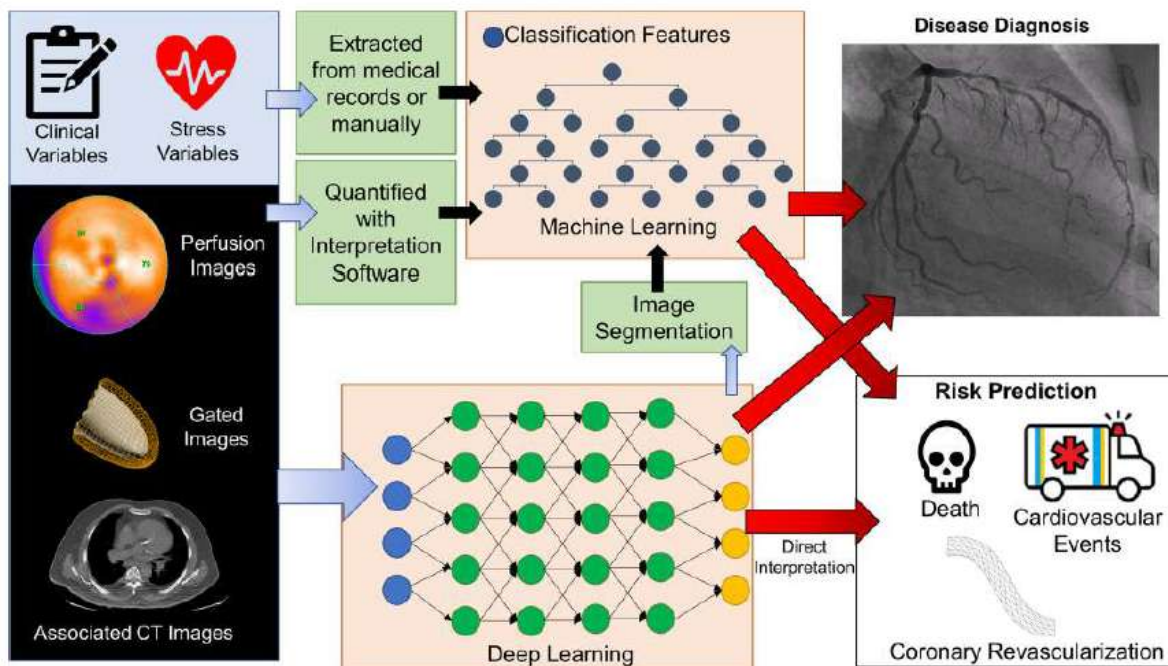
# ECG NN, Brain Maker



Study	Study type	Study population	Key findings
Smith et al. (2019)	Randomized Control	500 patients with CAD	AI-enhanced ECG significantly improved accuracy in detecting CAD compared to traditional ECG interpretation [75]
Zhang et al. (2019)	Prospective Cohort	800 patients with suspected heart disease	AI-enhanced ECG showed higher sensitivity and specificity in detecting myocardial infarction (heart attack) [76]
Chen et al. (2020)	Prospective Cohort	1200 asymptomatic individuals	AI-augmented ECG demonstrated higher sensitivity and specificity in predicting future cardiovascular events [77]
Park et al. (2020)	Randomized Control	1500 individuals with hypertension	AI-augmented ECG allowed early detection of hypertensive heart disease, facilitating personalized treatment plans [78]

Patel et al. (2021)	Retrospective	800 patients with heart failure	AI-assisted ECG provided real-time heart function monitoring, enabling personalized treatment adjustments [79]
Li et al. (2021)	Retrospective	600 patients with arrhythmias	AI-supported ECG interpretation demonstrated improved accuracy in identifying complex arrhythmia patterns [80]
Lee et al. (2022)	Meta-analysis	15,000 ECG records from diverse	AI interpretation demonstrated higher accuracy in detecting various arrhythmias compared to standard methods [81]
Chen et al. (2022)	Meta-analysis	10,000 diverse ECG records	AI-aided ECG analysis showed a significant reduction in false negatives, enhancing the detection of heart conditions [82]
Wang et al. (2023)	Cross-sectional	600 patients with suspected ACS	AI-augmented ECG expedited the diagnosis of acute coronary syndrome, leading to quicker intervention and care [83]
Kim et al. (2023)	Cross-sectional	400 elderly patients	AI-assisted ECG improved risk stratification for cardiovascular diseases in the elderly population [84]

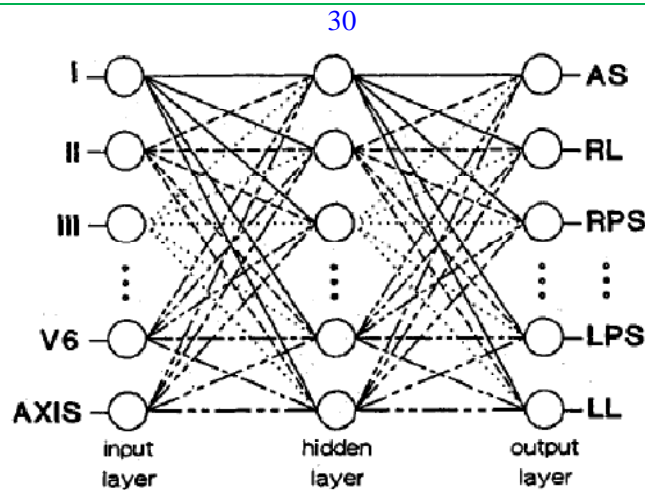
47



Outline of ML and DL approaches to disease diagnosis or risk prediction.



- ✓ Clinical and stress variables can be obtained from electronic medical records for use as classification features with machine learning.
- ✓ Imaging variables (including perfusion, functional, and computed tomography (CT) features) can be obtained from interpretation software.
- ✓ These classification features enable machine learning predictions for disease diagnosis or cardiovascular risk.
- ✓ Deep learning can be directly applied to images to provide image segmentation to quantify features for machine learning or provide direct predictions



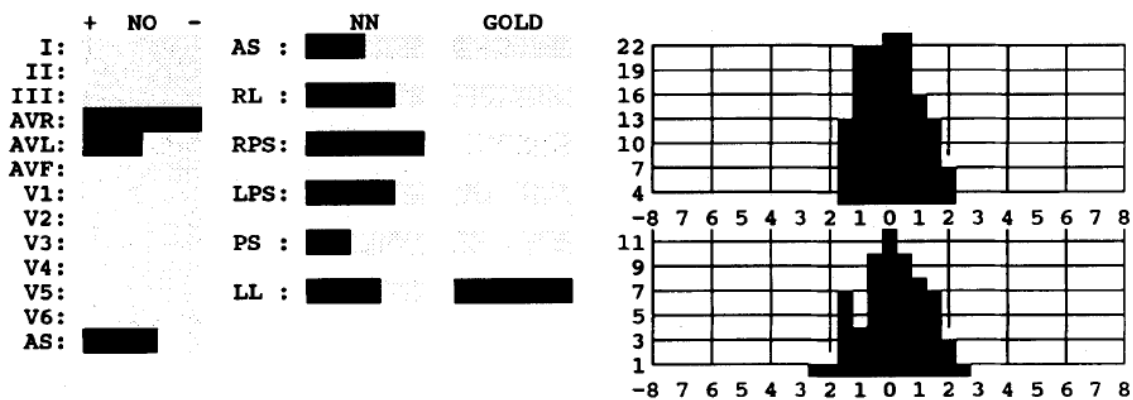
- ✓ Each input neuron at the left side represents the presence or absence and polarity of a delta wave in one lead.
- 13<sup>th</sup> neuron: axis of the QRS complex.
- six output neurons represent possible accessory pathway locations.
  - 🔔 AS = anteroseptal; RL = right lateral;
  - 🔔 RPS = right posteroseptal; PS = posteroseptal;
  - 🔔 LPS = left posteroseptal; LL = left lateral.

30

```

2:32 BrainMaker v2.0 Copyright(C)1989 California Scientific Software 0:00
System File Operate Options Display Print
Waiting Files: wpwnum2.srt Learn Rate: 1.000 Tolerance: .1
Fact: 1 Total: 1 Bad: 1 Last: 0 Good: 0 Last: 0 Run: 1

```



Layout of the standard output of the neural network.

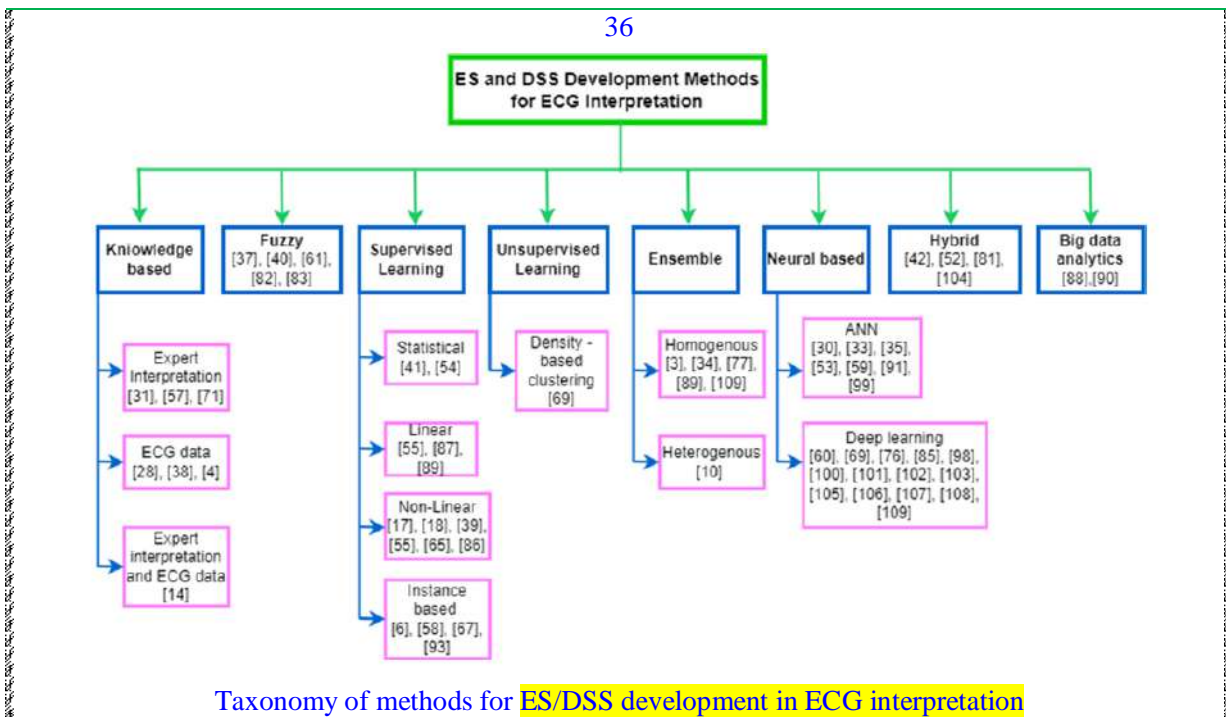
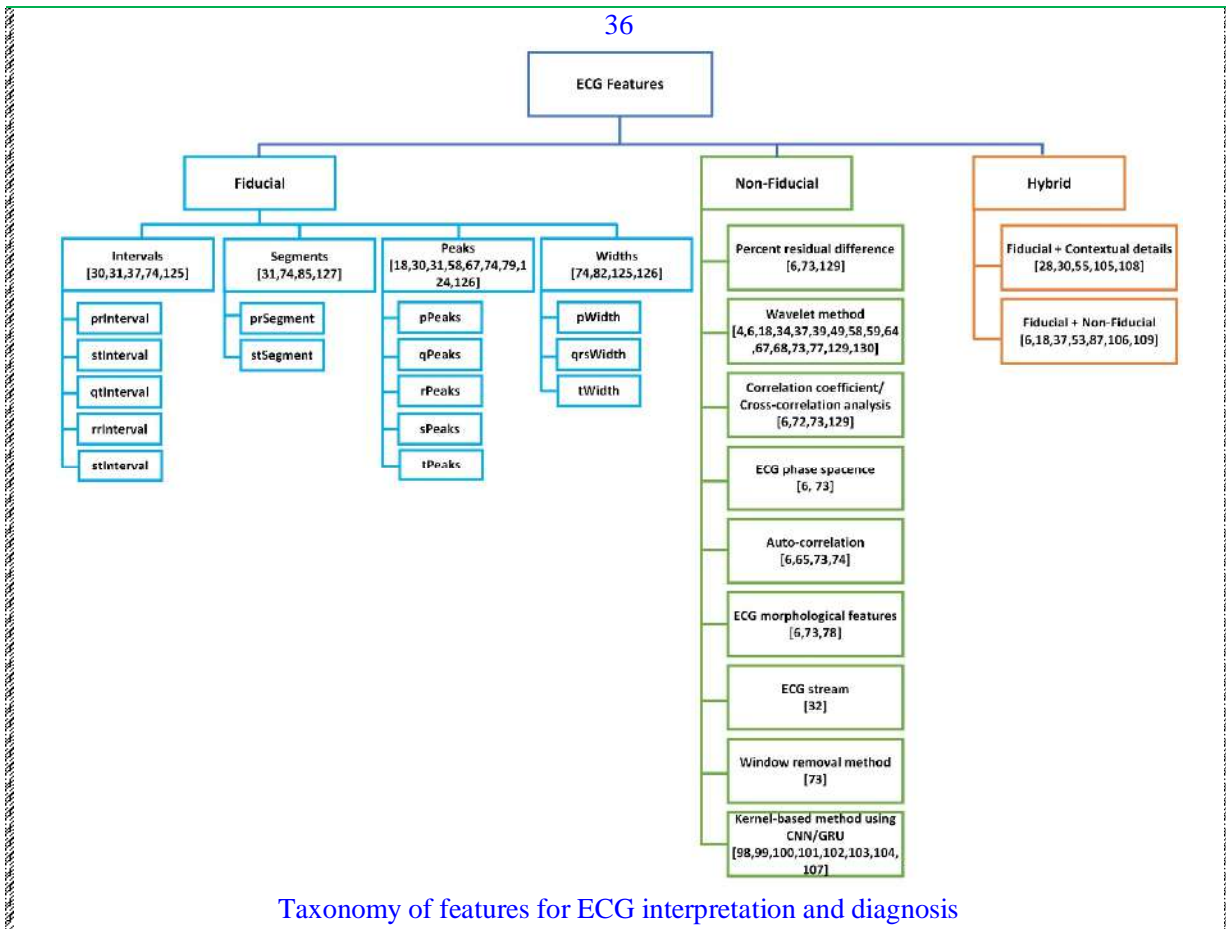
- ✓ The four top lines indicate the state of the network, what task it is presently performing, which files are used, etc.
- ✓ The left column shows the input: the presence or absence of delta waves and their polarity and the electrical axis of the QRS complex.
- ✓ The two columns in the middle (NN = neural network and gold) represent the output, to the left (NN) the output calculated by the neural network, to the right the gold standard (the location determined during surgery).
- ✓ The two bar charts to the right show histograms of the weight matrices of the hidden and output neurons.
- ✓ AS = anteroseptal; RL = right lateral; RPS = right posteroseptal; PS = posteroseptal;
- ✓ LPS = left posteroseptal; LL = left lateral.

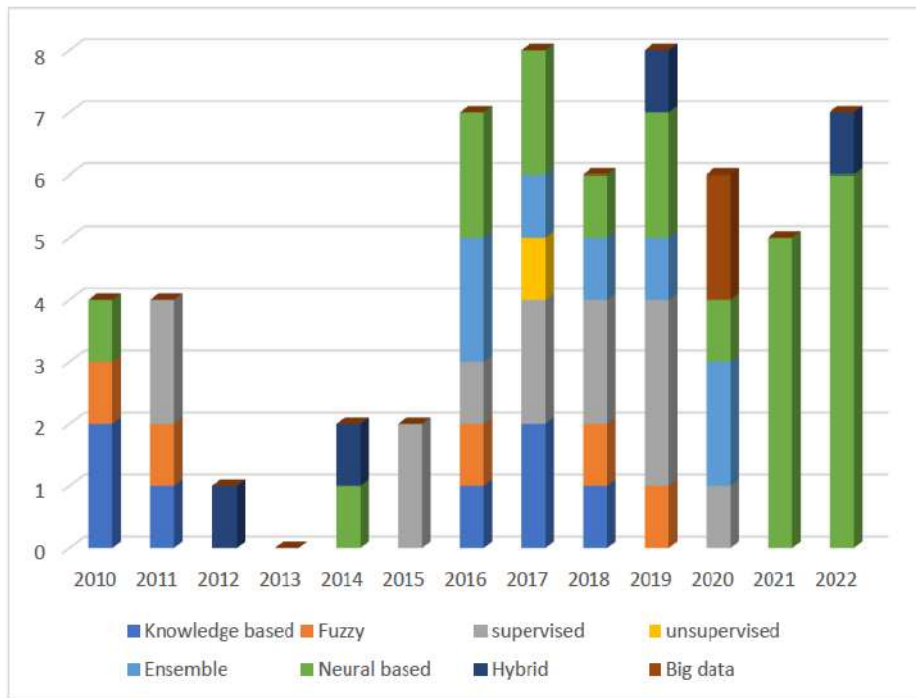
32



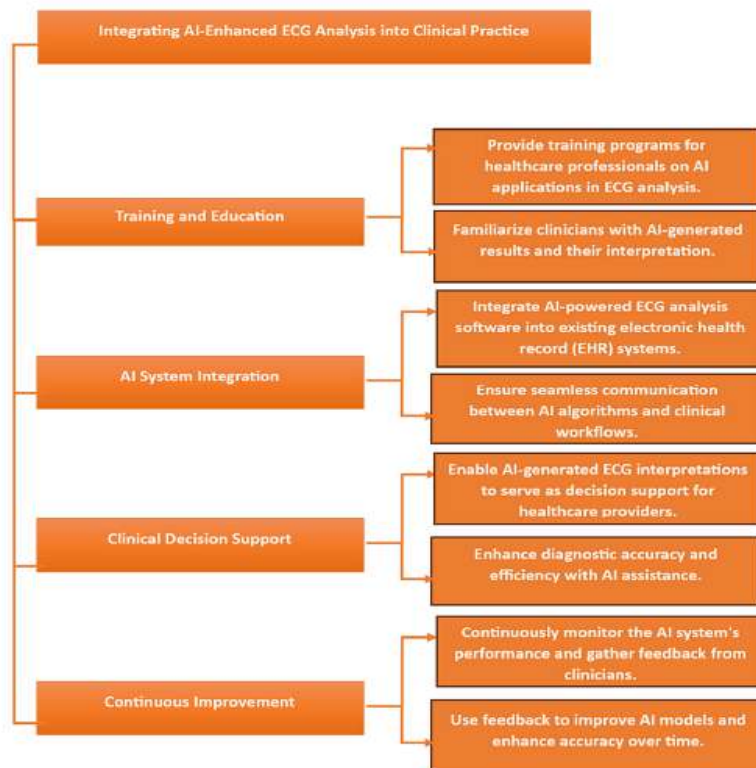
36

Title/App Name	Objective	Development Platform	Data Acquisition Interface	Measured Parameters	Heart Disorder Detected
kardiaMobile	Captures a medical-grade single lead ECG signal to detect heart rhythm	Android and iOS	Ultrasound	ECG traces, Heart rate	Atrial Fibrillation, bradycardia, tachycardia
kardiaMobile6L	Captures a medical-grade 6 lead ECG signal for comprehensive heart condition	Android and iOS	Ultrasound	Detailed ECG traces, Heart rate, weight, blood pressure	Atrial Fibrillation, bradycardia, tachycardia
Cardiax Mobile ECG	A companion application designed for cardiac health monitoring with 12 channels/ Lead	Windows and Android	Wi-Fi	ECG traces, Heart rate, QRS complex, Pd, PQ	Sinus Rhythm Arrhythmias
cardiolyse	A healthcare mobile application to connect with existing cardio appliance device	Java and Android	OTG USB cord	ECG traces and other 17 parameters	None
Beat2Phone	Mobile application for 1 lead ECG signals to monitor heart rate and posture	Android	Bluetooth	ECG traces, Heart rate, HRV, GPS location Timestamp	None
TouchECG	A 12-Lead Mobile application for interpreting ECG signals	Android	Bluetooth	ECG traces, heart rate	Arrhythmias

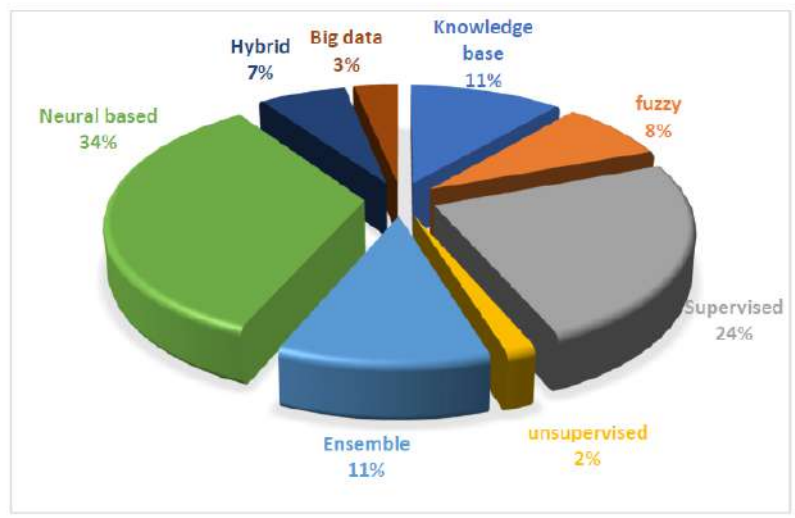




Trends in publications on ES/DSS-based ECG interpretations in the last decade

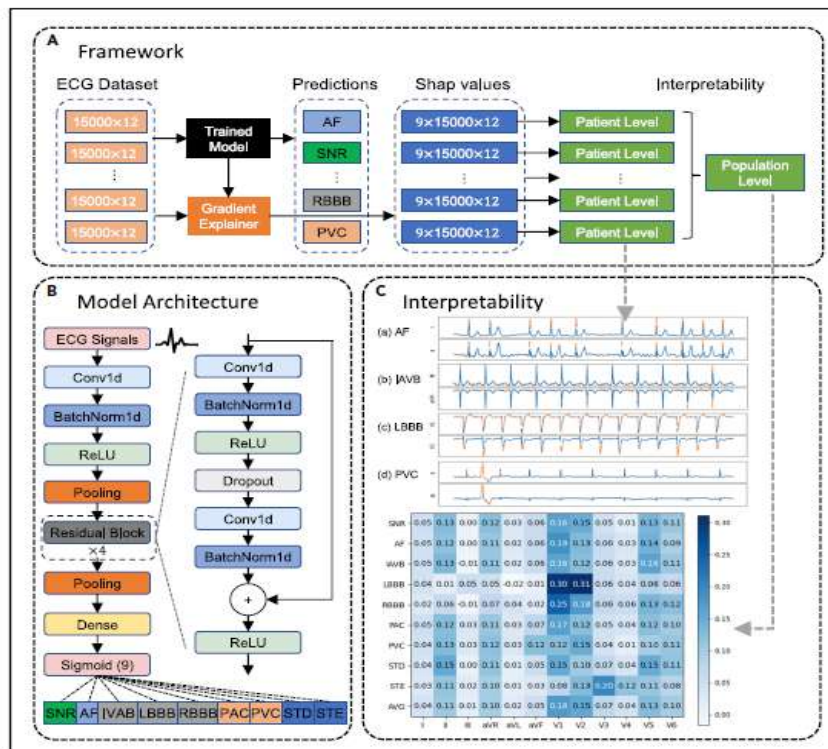


Integrating AI-enhanced ECG analysis into clinical practice

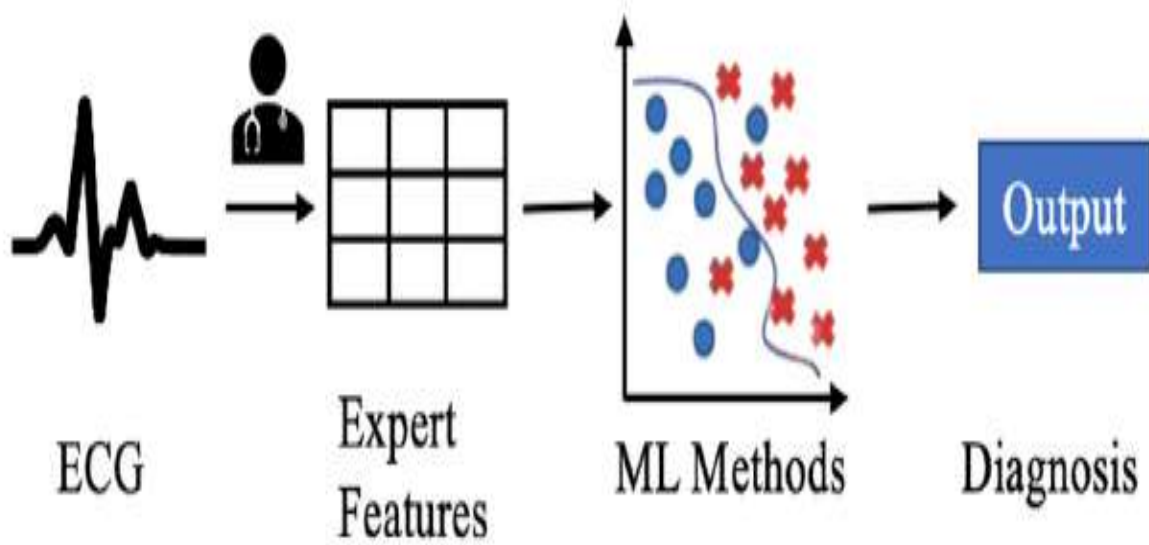


Percentage distribution of the methods for ES/DSS development for ECG interpretation.

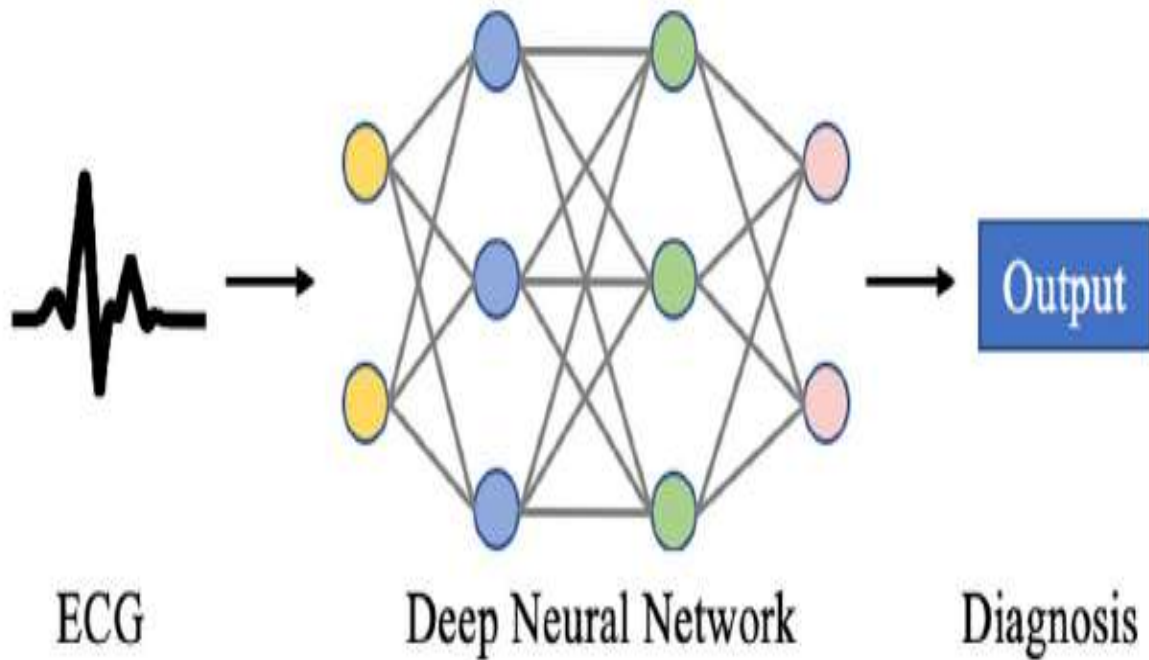
# CNN + Cardiology



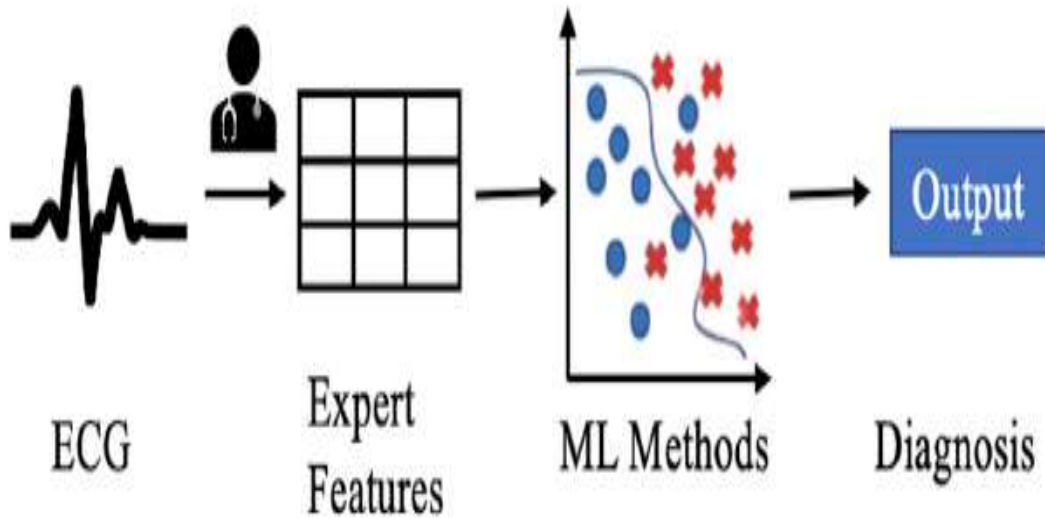
### A Traditional methods



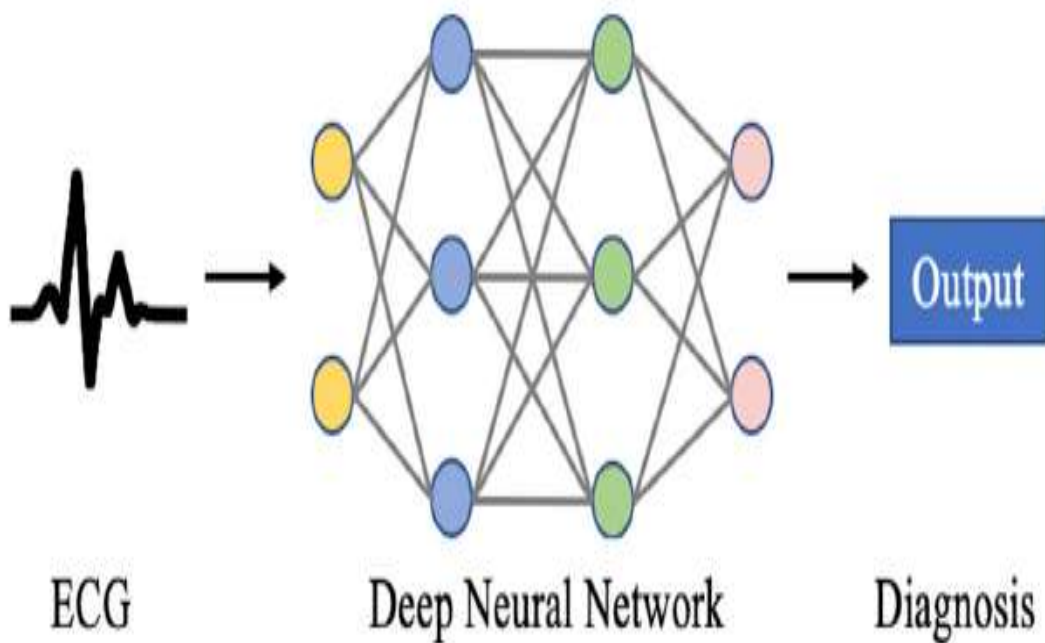
### B Deep learning methods



### A Traditional methods

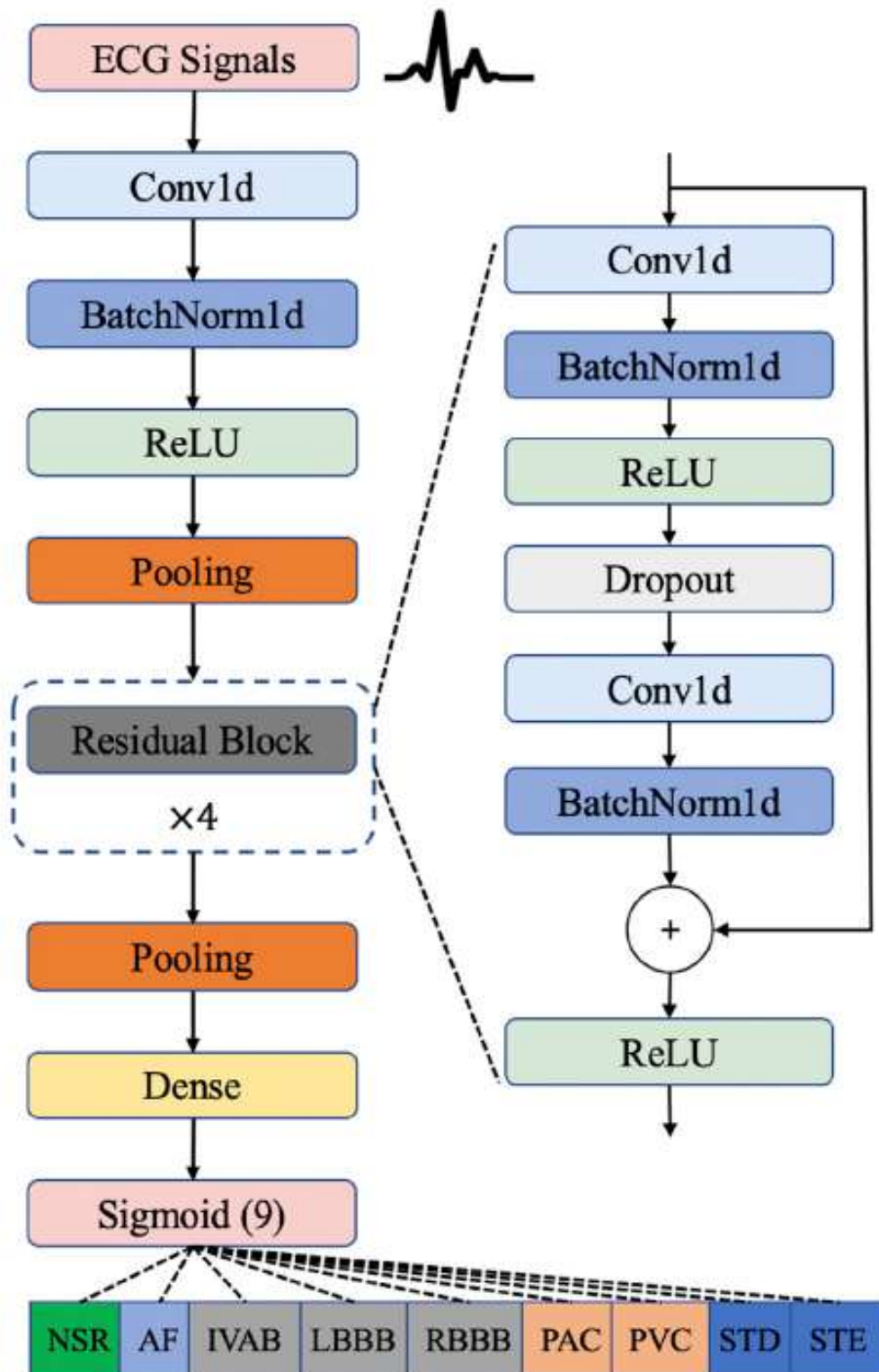


### B Deep learning methods



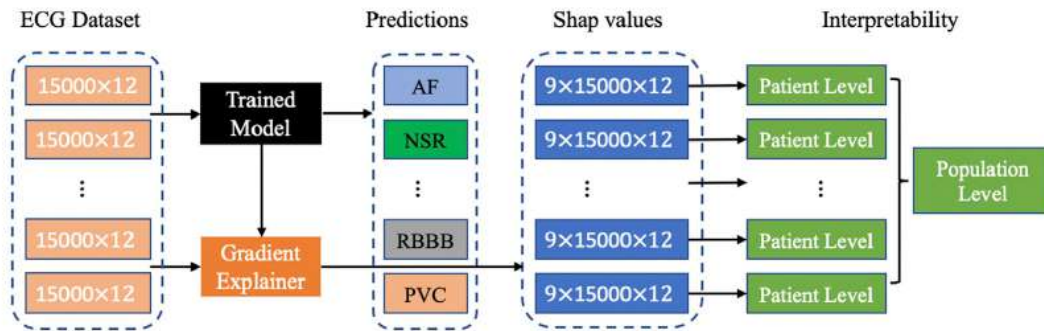
Comparison of existing models for automatic diagnosis of ECG abnormalities

(A) Two-stage traditional methods using feature engineering; (B) end-to-end deep learning methods

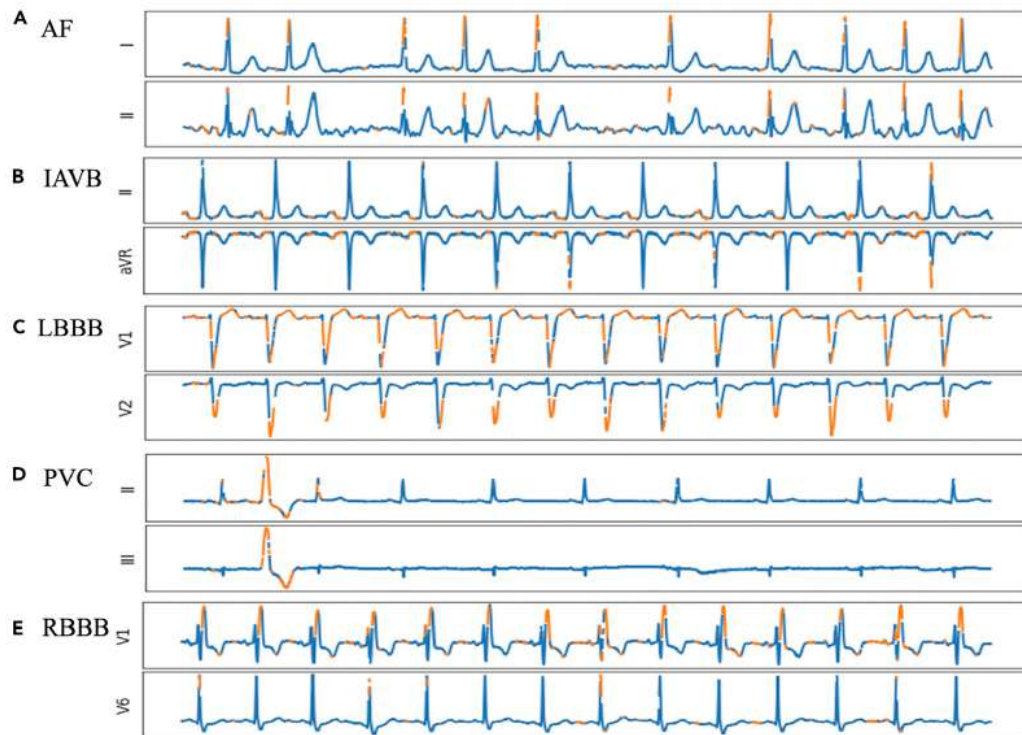


Deep neural network architecture for cardiac arrhythmia diagnosis

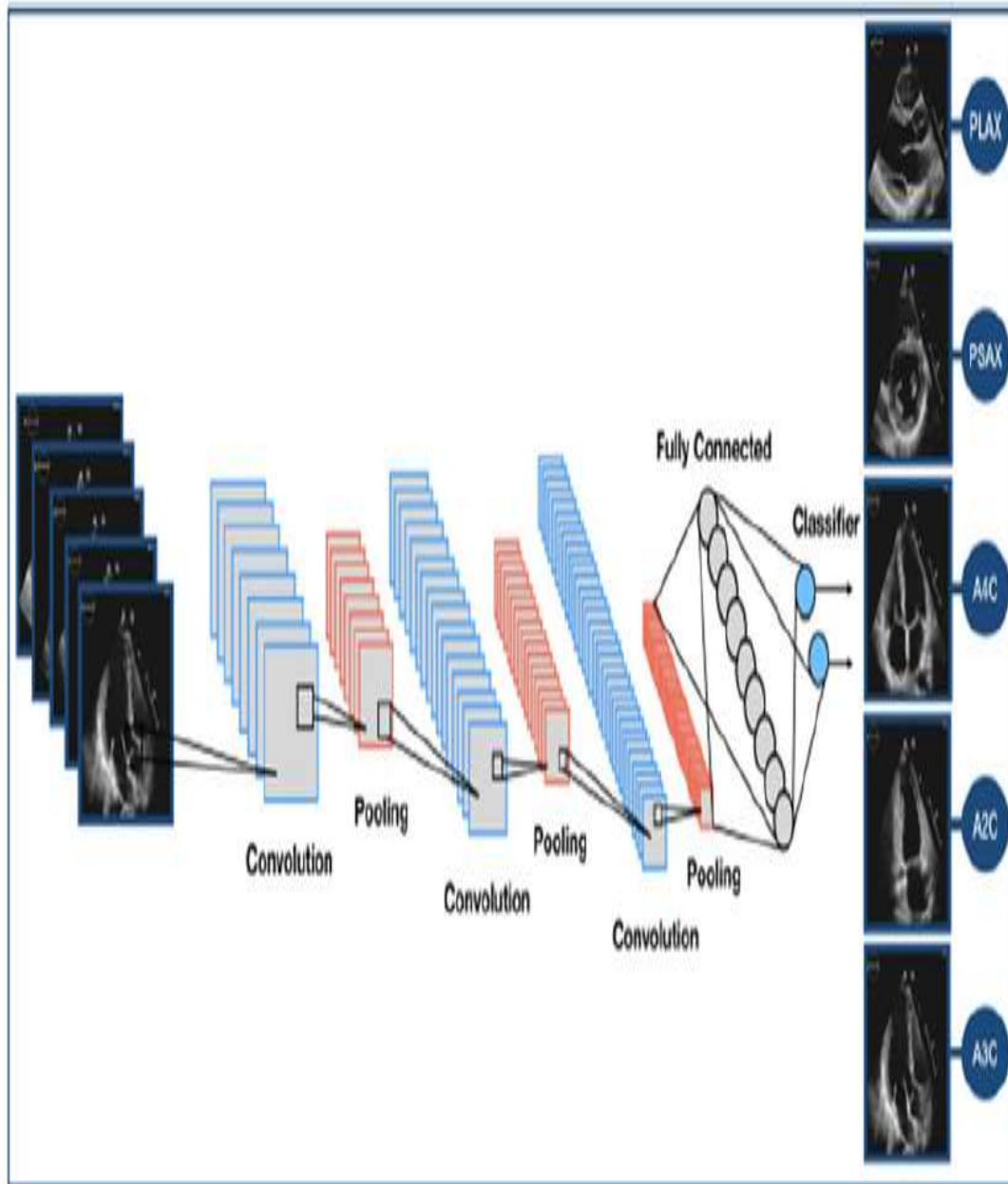




Interpretability of the deep learning model using SHAP values at both the patient level and population level

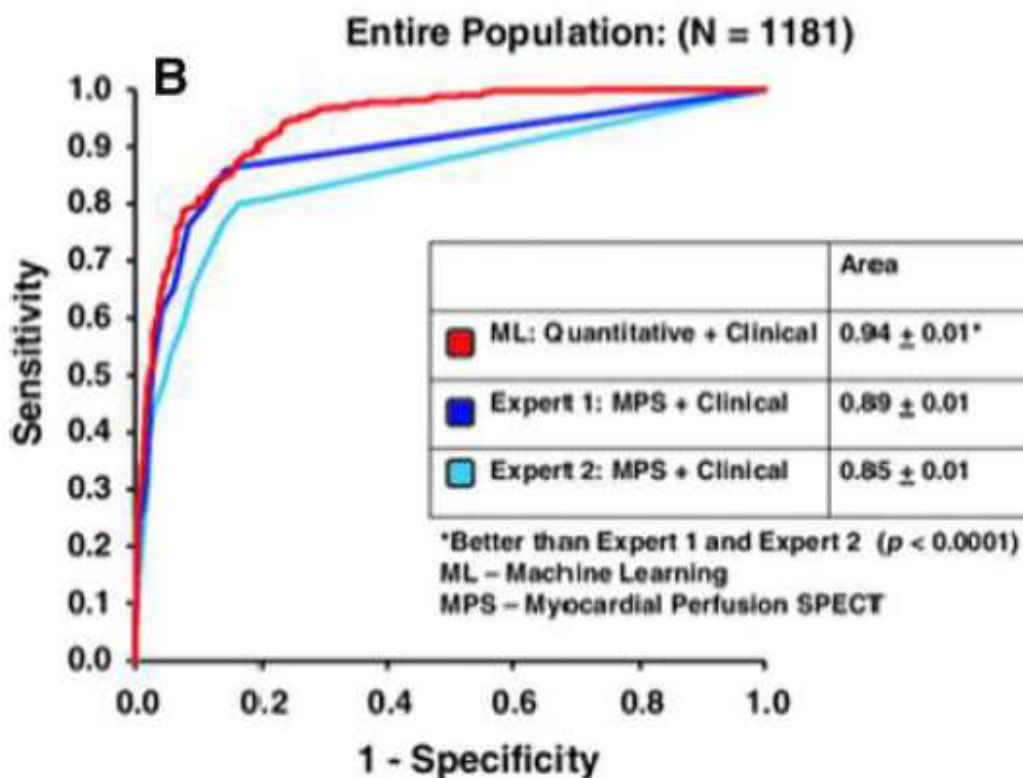
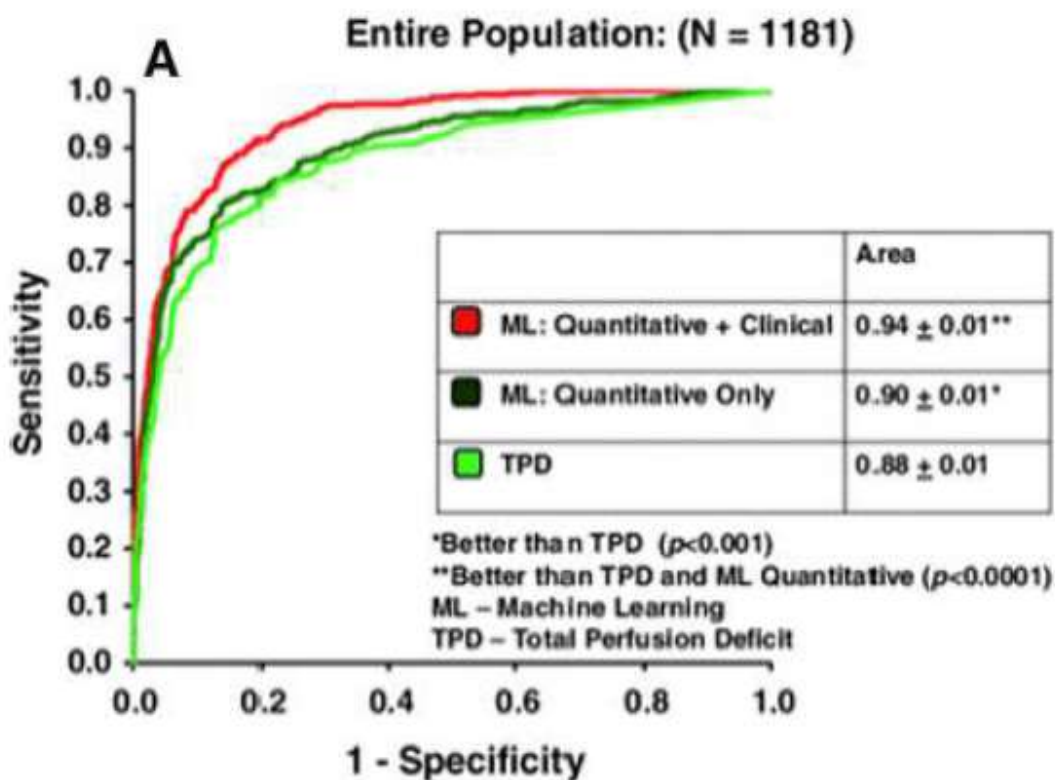


- ✓ Explanation of the model's prediction results for several ECG instances from different patients
- ✓ The features with high contribution (i.e., SHAP values) are highlighted in orange.
- ✓ Only the last 10 s of top 2 influential leads are displayed due to the limited space



A convolutional network model for AI based autonomous view classification,

- 🔔 Stepping stone for an eventual machine learning pipeline for automated diagnosis and disease surveillance.
- 🔔 From Alsharqi, et al. Echo Res Pract. 2018;5: R115–25, with permission

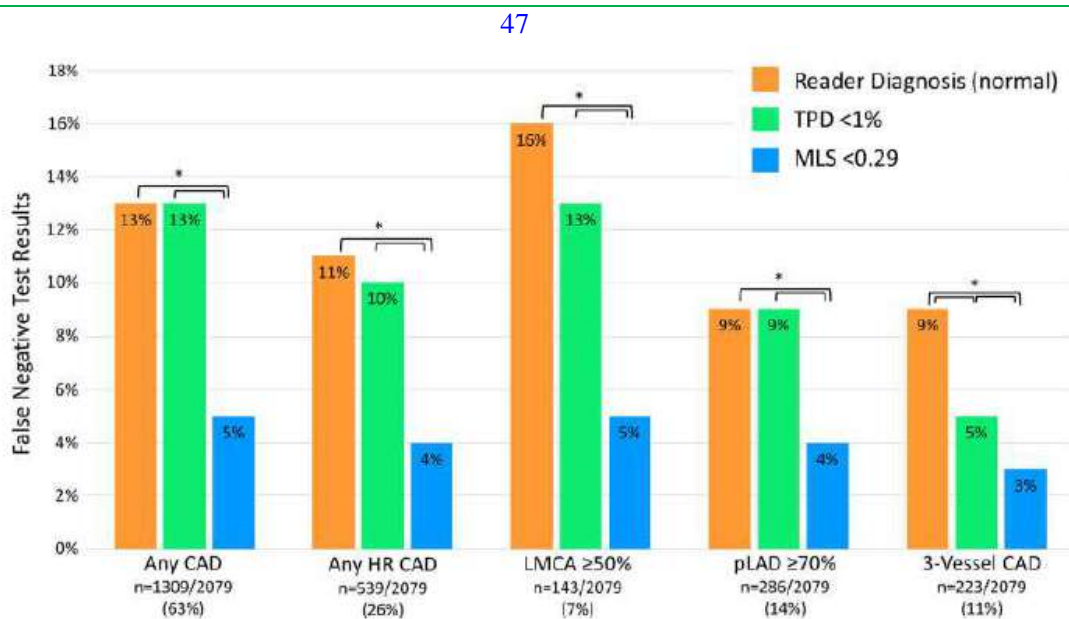


Machine learning for improving CAD diagnosis.

Machine learning-based integration of clinical and imaging information achieved higher diagnostic accuracy for detection of significant CAD than expert readers or TPD in a large population.

- ✓ Reprinted with permission: Arsanjani R, Xu Y, Dey D, et al Improved accuracy of myocardial perfusion SPECT for detection of coronary artery disease by machine learning in a large population. J NuclCardiol2013;20:553–62.17

## Diagnostic safety of a ML score



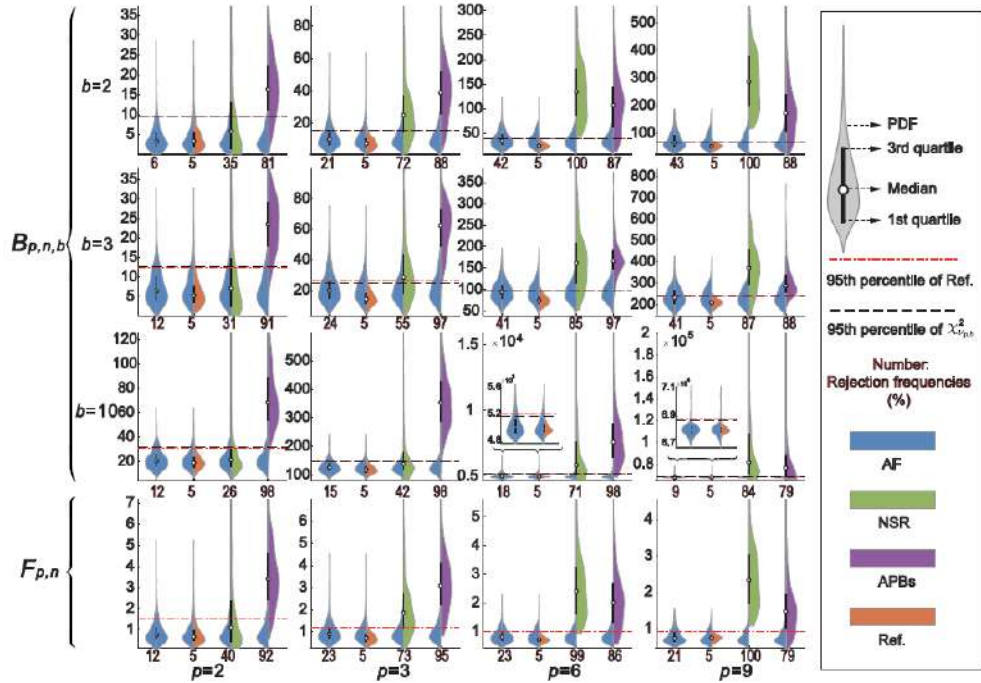
Diagnostic safety of a ML score (MLS) for automated cancelation of rest imaging.

- ✓ Frequency of false-negative test results among patients categorized as low-risk by expert visual interpretation (Reader Diagnosis), stress total perfusion deficit (TPD), and MLS.
  - ✓ Frequency of all categories of obstructive coronary artery disease (CAD) was significantly lower for patients identified as low-risk by MLS.
- LCx, left circumflex artery;
  - LMCA, left main coronary artery;
  - pLAD, proximal left anterior descending artery;
  - RCA, right coronary artery;
  - TPD, total perfusion deficit

Ref: Journal of Nuclear Cardiology, Eisenberg et al., Diagnostic safety of a machine learning-based automatic patient selection algorithm for stress-only myocardial perfusion SPECT, Epub ahead of print, (2021),

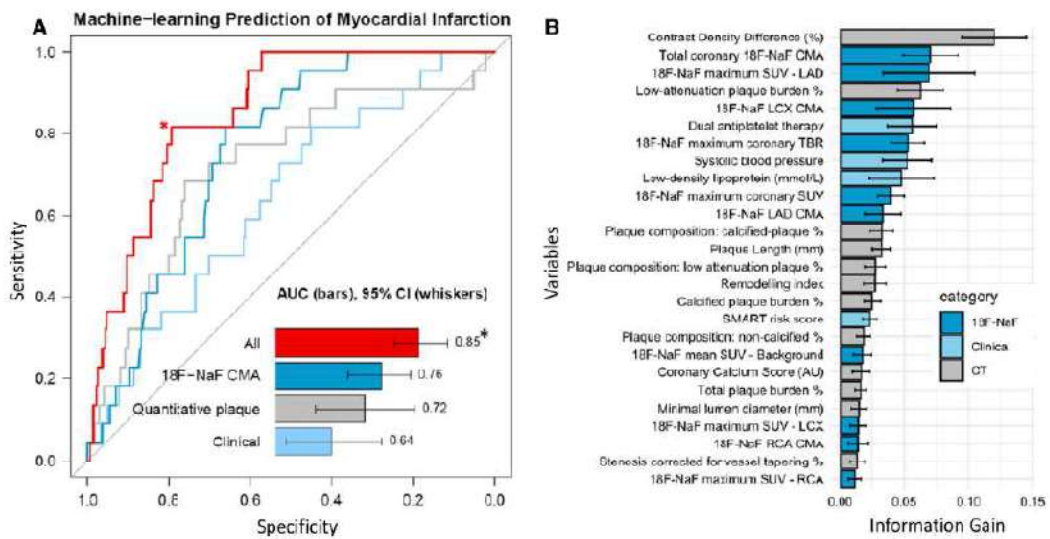
# Accuracy Complexity

53



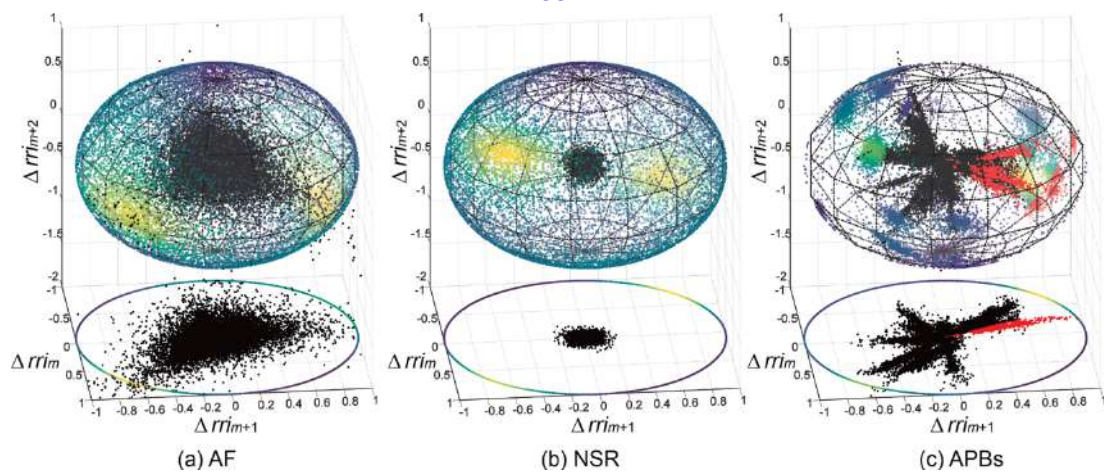
Violin plots of Sobolev test statistics based on  $\Delta$ RRI Poincaré plots.

47



- ✓ Panel A shows that the prognostic accuracy of the ML model incorporating all available information was higher compared to the imaging components in isolation.
- ✓ Panel B outlines feature importance, highlighting the potential gains in accuracy from combining multimodality imaging information with clinical variables.
- This research was originally published in JNM. Kwiecinski et al. Machine Learning with 18F-Sodium Fluoride PET and Quantitative Plaque Analysis on CT Angiography for the Future Risk of Myocardial Infarction. J Nucl Med. 2022;631:158-165. SNMMI
- 🔔 Kwiecinski et al. developed a machine learning algorithm that integrated clinical factors, computed tomographic plaque characteristics, and 18F-sodium fluoride positron emission tomography quantitation to predict risk of myocardial infarction

53



Spherical and circular projections of  $\Delta RRI$  Poincaré plots for AF, NSR, and APBs.

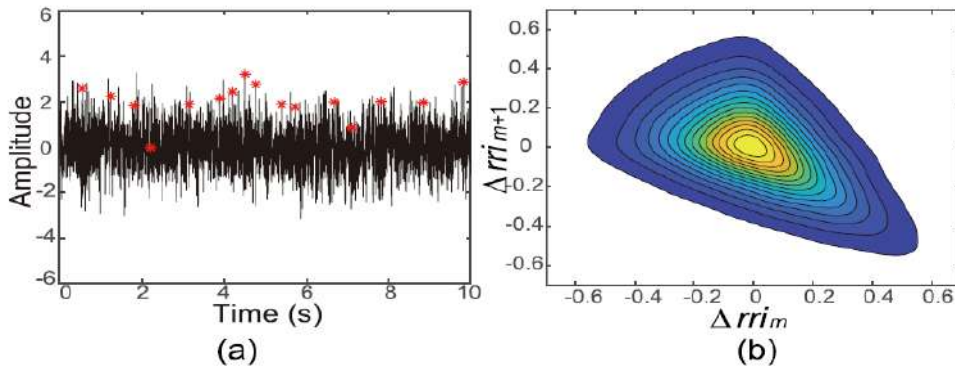
- ✓ The upper half shows the three-dimensional Poincaré plot its projection onto the spherical surface,
- ✓ Lower half shows the two-dimensional Poincaré plot and its projection onto the circular surface of  $\Delta RRI$ . (a) AF; (b) NSR; (c) APBs.

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Comparison of four-class classification performance with other methods.

Author	Method	F1(%)			
		AF	NSR	O	~
Teijeiro et al., 2018	Engineered features + LSTM (ECGs)	85.5	90.3	73.7	56.2
Sadr et al., 2018	Engineered features (RRIs)	75.0	90.0	68.0	32.0
Hong et al., 2019	Engineered features + CNN (ECGs)	81.3	91.2	75.1	56.7
Fang et al., 2021	Engineered features + CNN (ECGs)	83.0	90.0	75.0	—
Our	MB (RRIs)	85.3	88.5	71.4	41.6

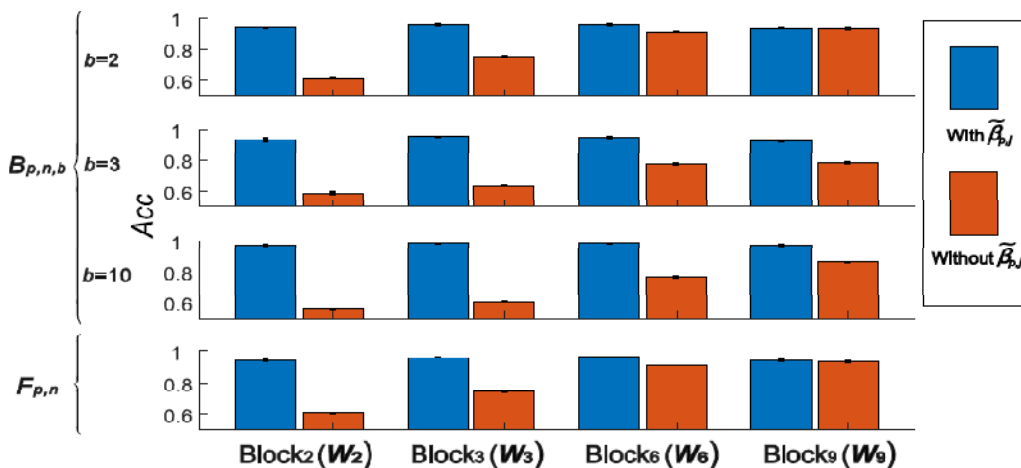
53



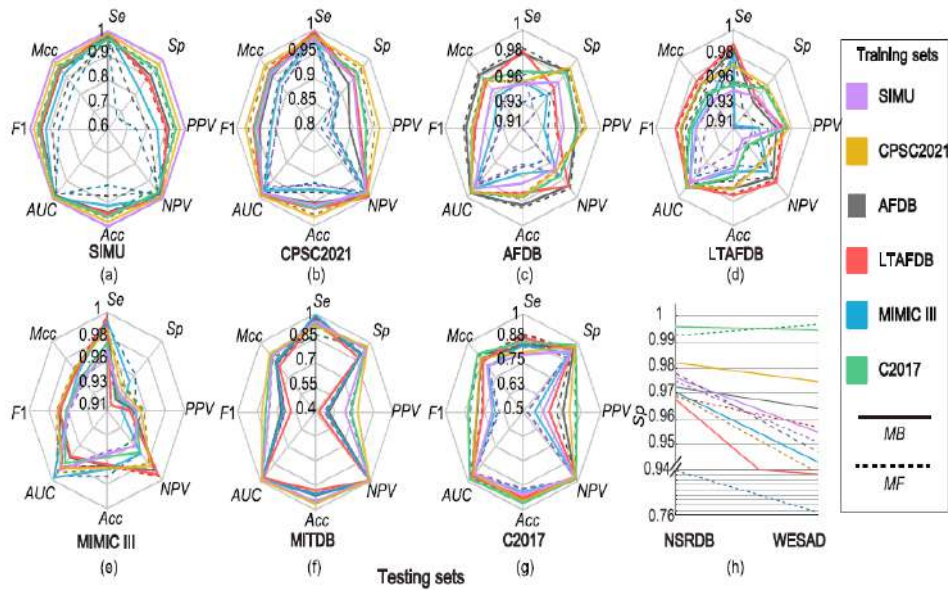
R-peak detection and pseudo-ΔRRI Poincaré plot under noise conditions.

- ✓ (a) R-peak detection in random noise; (b) Contour plot of the pseudo-ΔRRI Poincaré plot generated by noise

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Comparative Accs of single-block models with fixed  $W_p$ ,



### Cross-dataset validation results.

- ✓ Each octagon represents a particular testing database, and a corner of each octagon represents a specific performance metric. (a) SIMU; (b) CPSC2021; (c) AFDB; (d) LTAfDB; (e) MIMIC III; (f) MITDB; (g) C2017; (h) NSRDB and WESAD.

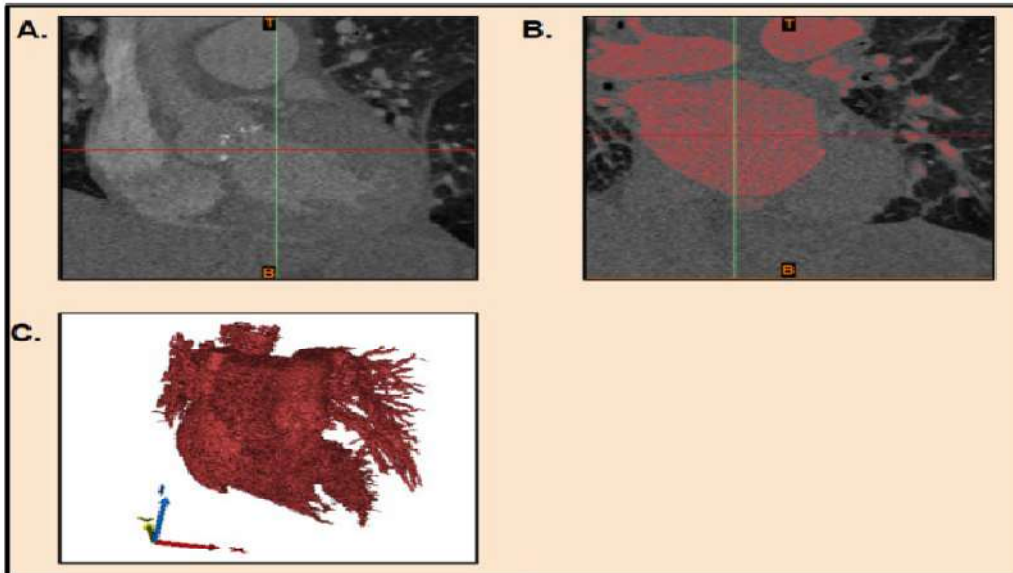
### Complexity and parameters of the proposed model.

Module		Complexity (FLOPs)	# Parameters
Block <sub>p</sub>	CONV <sub>p,j</sub>	$\mathcal{O}(Np^2n)$	$Np^2 + 1$
	S_Pool <sub>p</sub> (MB)	$\mathcal{O}(Nbn^2 + Npn^2)$	0
	S_Pool <sub>p</sub> (MF)	$\mathcal{O}(Npn^2)$	0
Batch Normalization		$\mathcal{O}(NM)$	$2N(M-1)$
MLP		$\mathcal{O}(N^2M^2 + NMC)$	$C +$ $(NM - N + 1 + C)[N(M-1)/2]$
Total	MB	621.45 K	1,770
	MF	357.39 K	1,770



# Segmentation Classification

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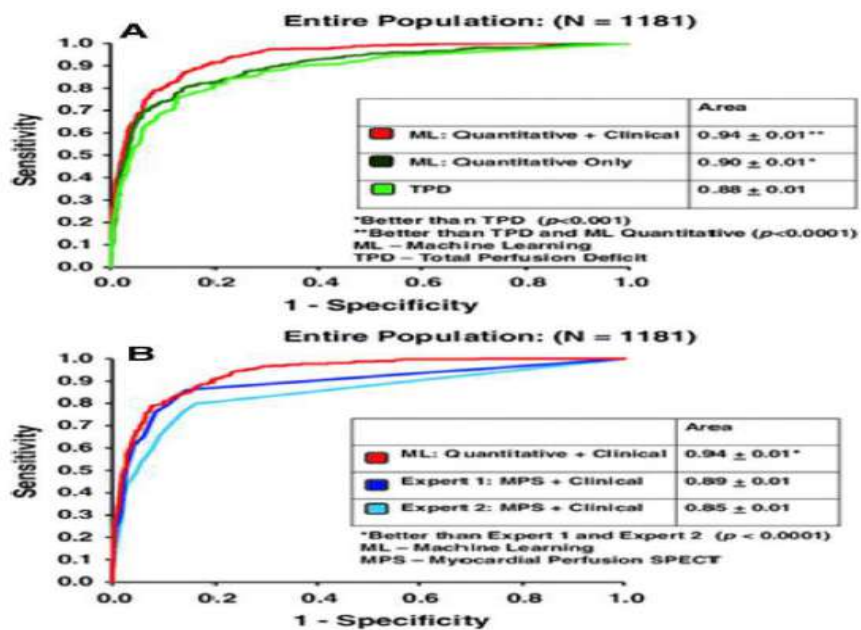
Rough depiction of the process of image segmentation.

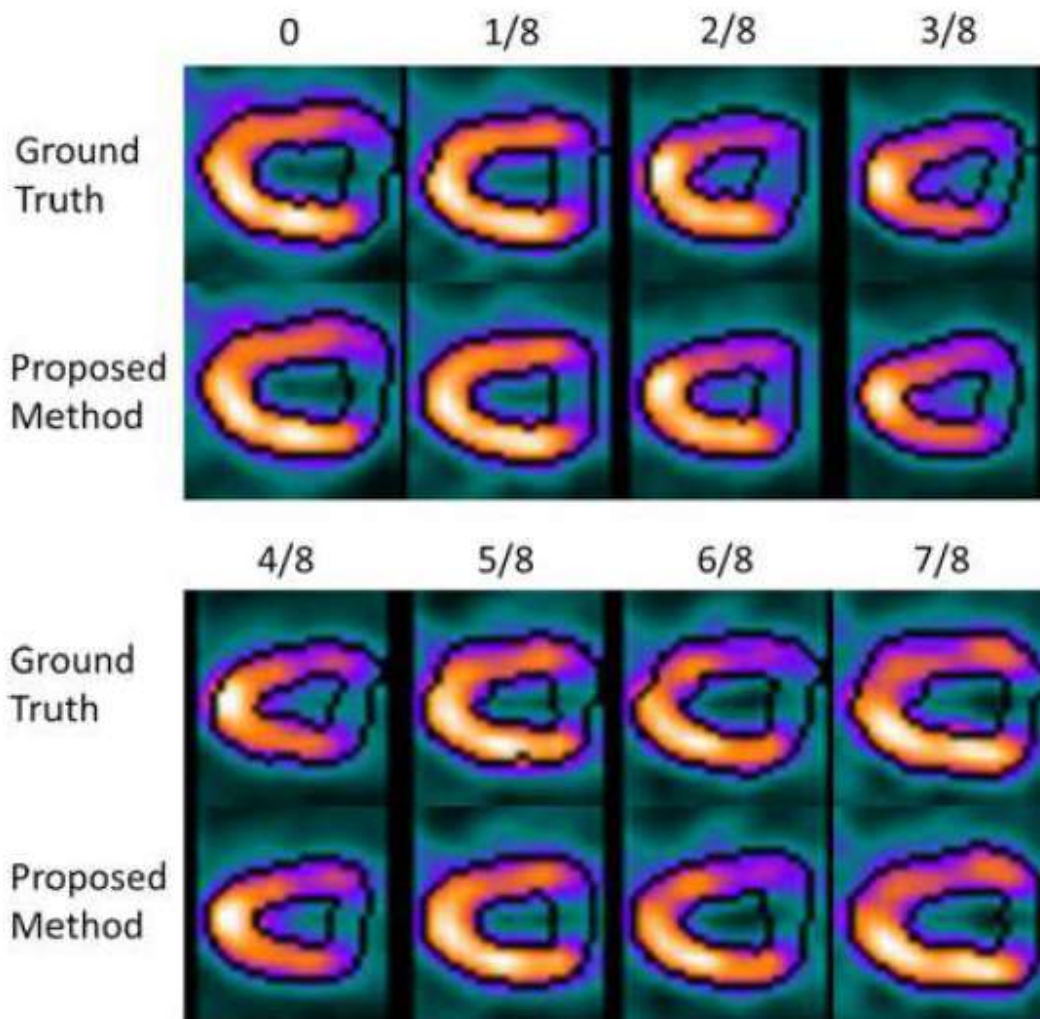
A) Displays the original DICOM image of the cross-section of the heart, supplied by Mimics Materialize. Student Edition.

B) Displays the mask made from a selection of target regions.

C) Displays the calculated 3D geometry to be meshed

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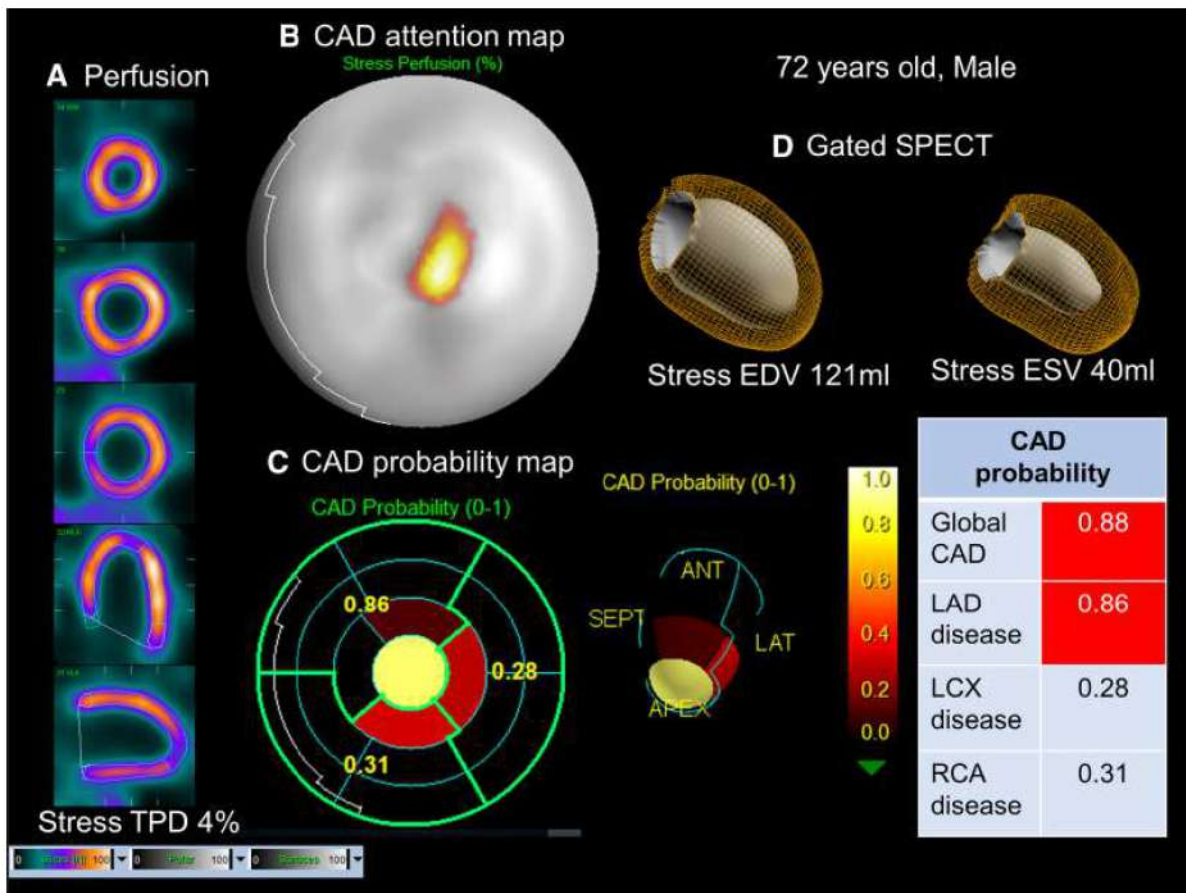




**Deep learning-based LV segmentation in MPI.**

- ✓ The axial views of patient #33 (abnormal) at different slices of gating phase 0 with segmentations of ground truth and proposed method.
- ✓ The black lines indicate the contours of endocardial and epicardial surface.
  - ! Ref Wang T et al, A learning-based automatic segmentation and quantification method on left ventricle in gated myocardial perfusion SPECT imaging: a feasibility study, J NuclCardiol 2020;27:976–987



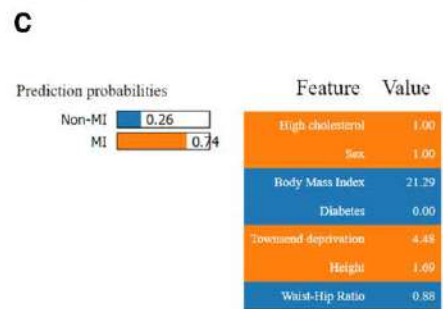
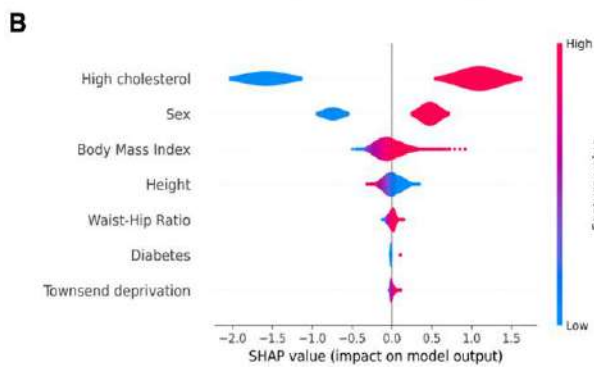
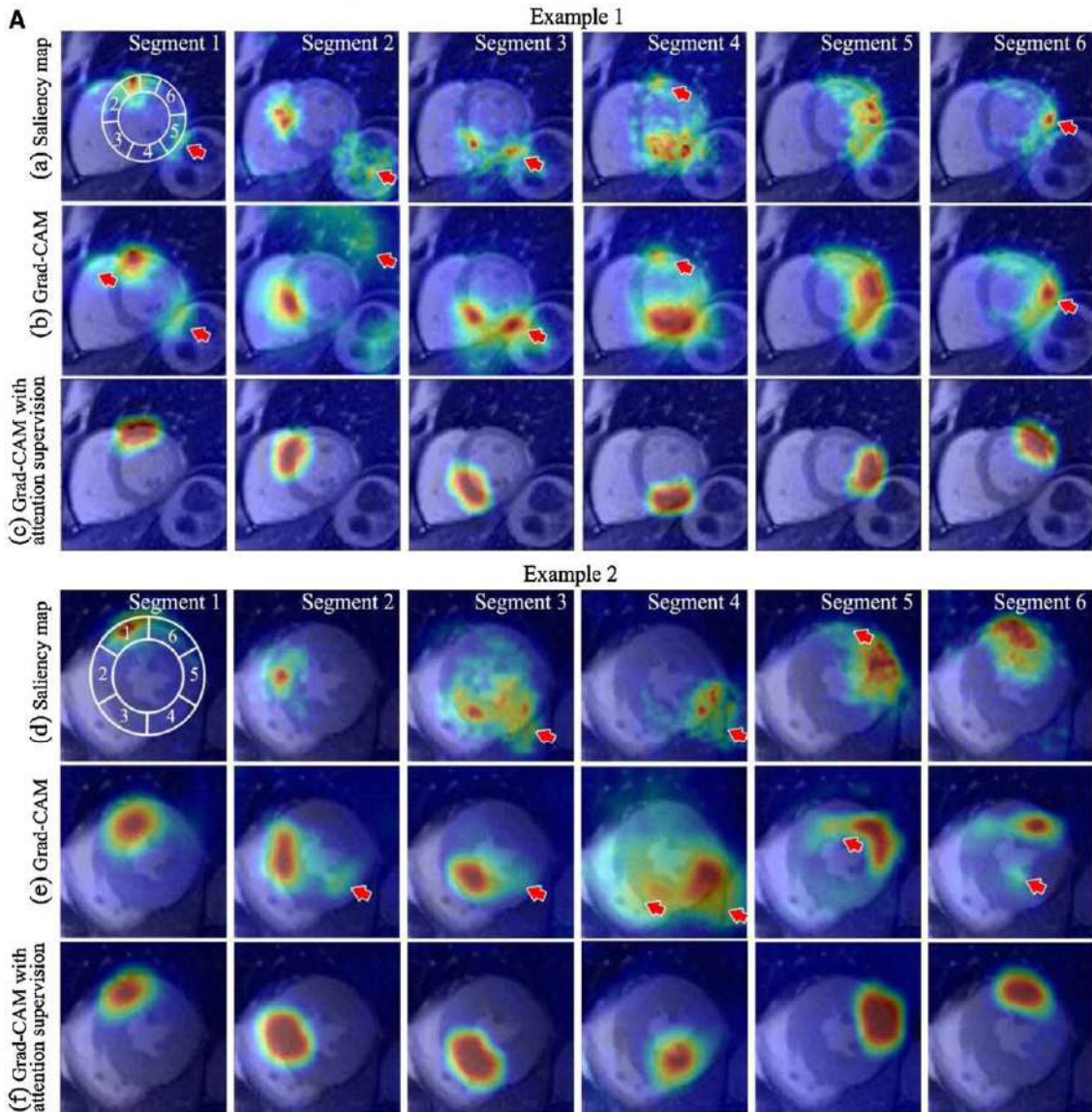


#### Deep learning with explainable artificial intelligence for CAD detection.

- + CAD-DL model trained on full spectrum of SPECT polar maps (perfusion, wall motion, and wall thickening) and variables obtained automatically from image data (age, sex, and LV volumes) has been shown to out-perform quantitative stress TPD and expert reader diagnosis.
- ✓ Architecture includes generation of “CAD attention maps” providing visualization of DL-based rationale for predictions—
- 🔔 Explainable AI. This example shows 72-year-old male with 85% stenosis in proximal left anterior descending (LAD).
  - a. Stress images, with visual assessment interpreted as equivocal.
  - b. CAD attention map highlighting image regions contributing to prediction.
  - c. CAD probability map showing a high probability of LAD disease.
  - d. LV volumetrics.

Ref: Otaki Y et al Clinical Deployment of Explainable Artificial Intelligence of SPECT for Diagnosis of Coronary Artery Disease. JACC: Cardiovasc Imaging. 2021.

<https://doi.org/10.1016/j.jcmg.2021.04.030.19>



**Clinical examples and interpretation.**

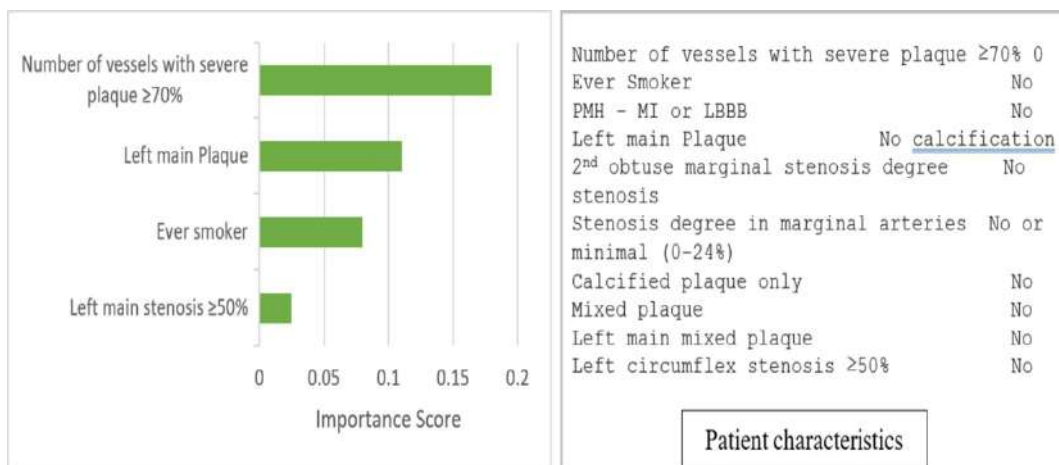
A: Attention map generated by gradient-weighted class activation mapping (Grad-CAM) and saliency in cardiac T1 mapping.

B: Global list of informative predictors from Shapley additive explanations (SHAP). High cholesterol,

sex, and body mass index are contributing positively to model output (myocardial infarction [MI]) while height contributes negatively (non-MI).

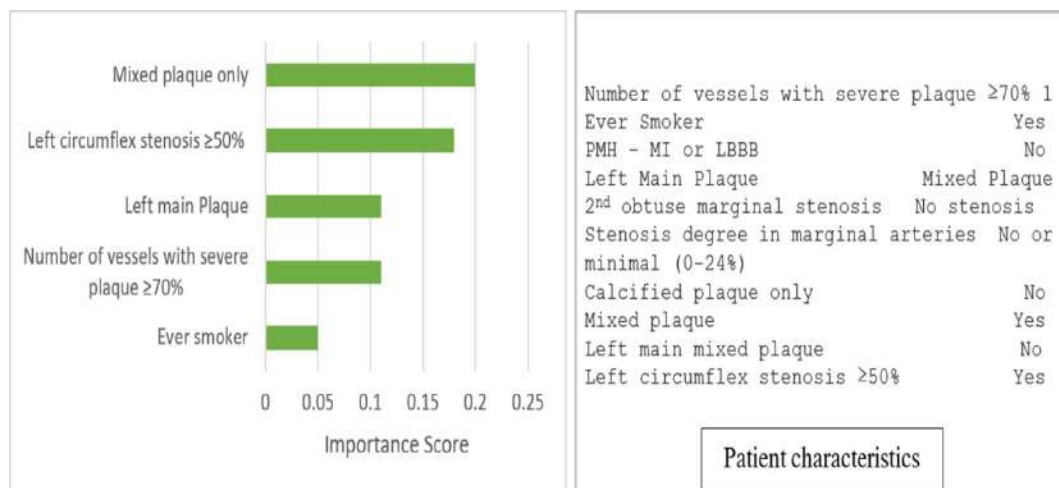
C: Local features contributions for a specific subject in the model. It shows the prediction probability for each class the subject might belong to. The color indicates whether the feature contributes to MI or non-MI classes while the numbers in the table represent the effect size in the model.

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LIME explanation for a correctly predicted patient with a low risk of MACE

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LIME explanation for a correctly predicted patient with a high risk of MACE

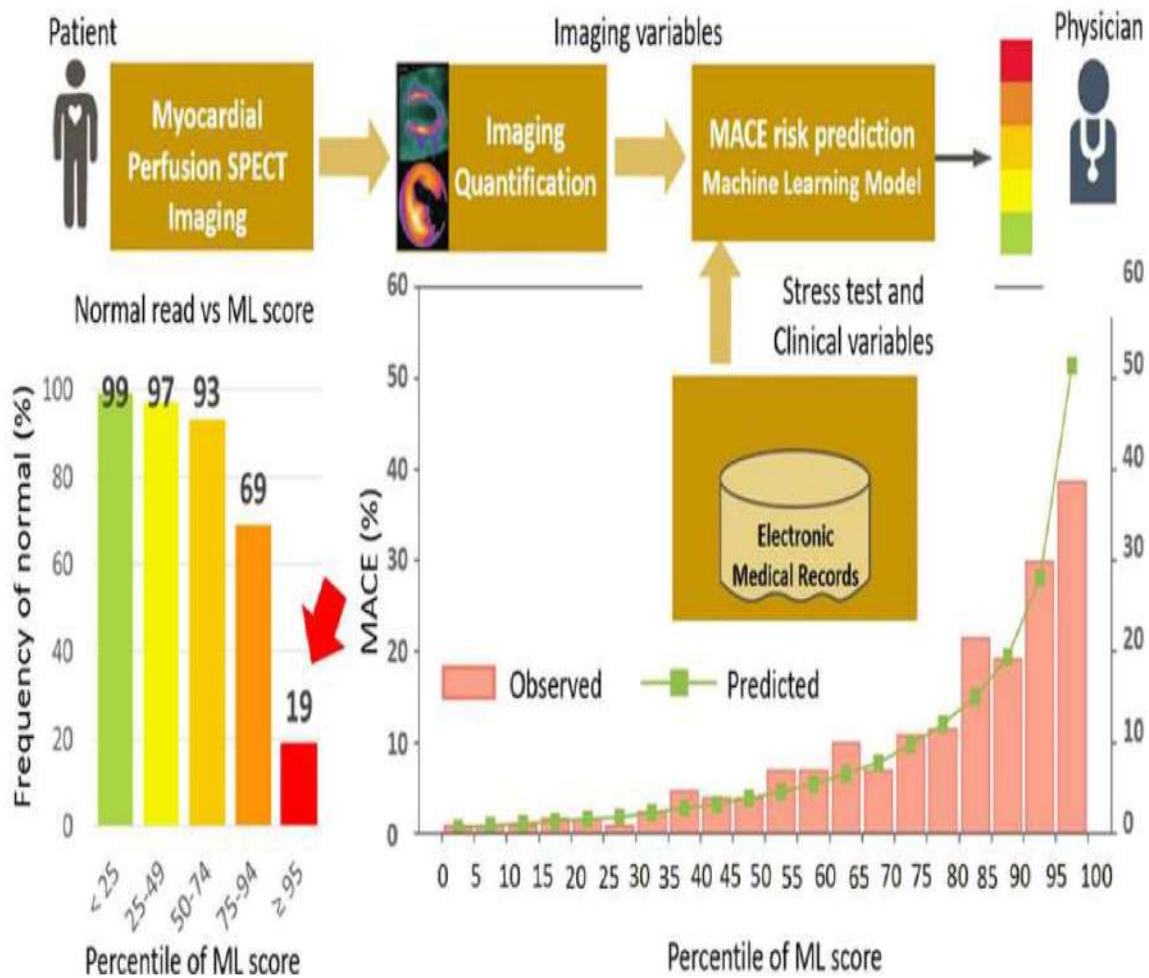
XAI	Aim	Properties	Input	Model	Application
PDP <sup>25</sup>	Shows the marginal effect of 1 or 2 predictors on the outcome	G, A	*	M, D	None
ALE <sup>26</sup>	Shows the average effect of features on the outcome	G, A	*	M, D	None
Class activation map <sup>20</sup>	Build discriminative image regions to show the regions used by the model	L, S	†	D	Classification <sup>27</sup> ; Regression <sup>28</sup>
RxREN <sup>29</sup>	Extract rules that drive the model using classified and misclassified data	G, S	*	D	None
NNKX <sup>30</sup>	Knowledge extraction from multilayers trained model	L, S	*	D	None
SHAP <sup>31</sup>	Provide feature importance list locally and globally based on game theory	G, L, A	*†	M, D	Classification <sup>32-34</sup> ; Regression <sup>35</sup>
LIME <sup>36</sup>	Explain the contribution of each feature toward the outcome for one single instance	L, A	*†	M, D	None
Layer-wise relevance propagation <sup>37</sup>	Generate a heat map in the input space to reveal the contribution of each voxel in the model outcome	L, S	†	D	None
Guided backpropagation <sup>38</sup>	Visualize the learning of the intermediate layer of deep learning models	L, S	†	D	Segmentation <sup>39</sup> ; Classification <sup>40</sup>
DeepLIFT <sup>41</sup>	Shows the additive features attribution to the model outcome	L, S	*†	D	None

Seq2Seq <sup>42</sup>	Visualize and debug sequence-to-sequence tool	L, S	*†	D	None
SmoothGrad <sup>19</sup>	Improve the sensitivity maps generated on the input image by removing the noise	L, S	†	D	Classification and Regression <sup>43</sup>
Saliency maps <sup>21</sup>	Generate saliency maps, which shows the contribution of each pixel toward the model output	L, S	†	D	Classification <sup>18</sup>
DeepTaylor <sup>44</sup>	Generate heat maps, which shows the contribution of each pixel toward the model output	L, S	†	D	None
DeConvNet <sup>45</sup>	Generate heat maps, which shows the contribution of each pixel toward the model output	L, S	†	D	None
Pattern attribution <sup>46</sup>	Generate heat maps, which shows the contribution of each pixel toward the model output	L, S	†	D	None
Integrated gradients <sup>47</sup>	Generate heat maps, which shows the contribution of each pixel toward the model output	L, S	†	D	None
Grad-CAM <sup>16</sup>	Generate heat map, which shows the contribution of each pixel toward the model output	L, S	†	D	Classification <sup>18,24,40,48,49,50</sup> ; Segmentation <sup>51</sup>
Grad-CAM++ <sup>52</sup>	Improved version of Grad-CAM	L, S	†	D	None
TCAV <sup>53</sup>	Features attribution	L, S	†	D	Classification <sup>54</sup> ; Segmentation <sup>55</sup>

A indicates agnostic; ALE, accumulated local effects; D, deep learning; DeConvNet, deconvolution network; DeepLIFT, deep learning important features; G, global; Grad-CAM, gradient-weighted class activation mapping; L, local; LIME, local interpretable model-agnostic explanations; M, machine learning; NNKX, neural network knowledge extraction; PDP, partialdependence plot; RxREN, rule extraction by reverse engineering; S, specific; Seq2Seq, sequence-to-sequence models; SHAP, Shapley additive explanations; TCAV, testing with concept activation vectors; and XAI, explainable artificial intelligence.

# Major adverse cardiac events (MACE)

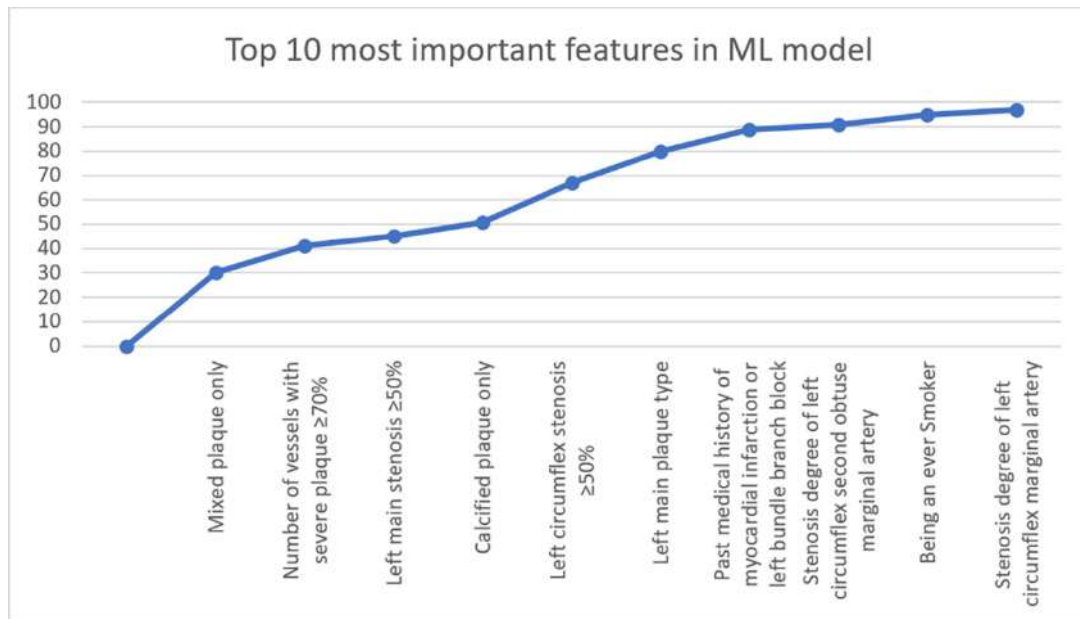
42



## Prediction of MACE by machine learning.

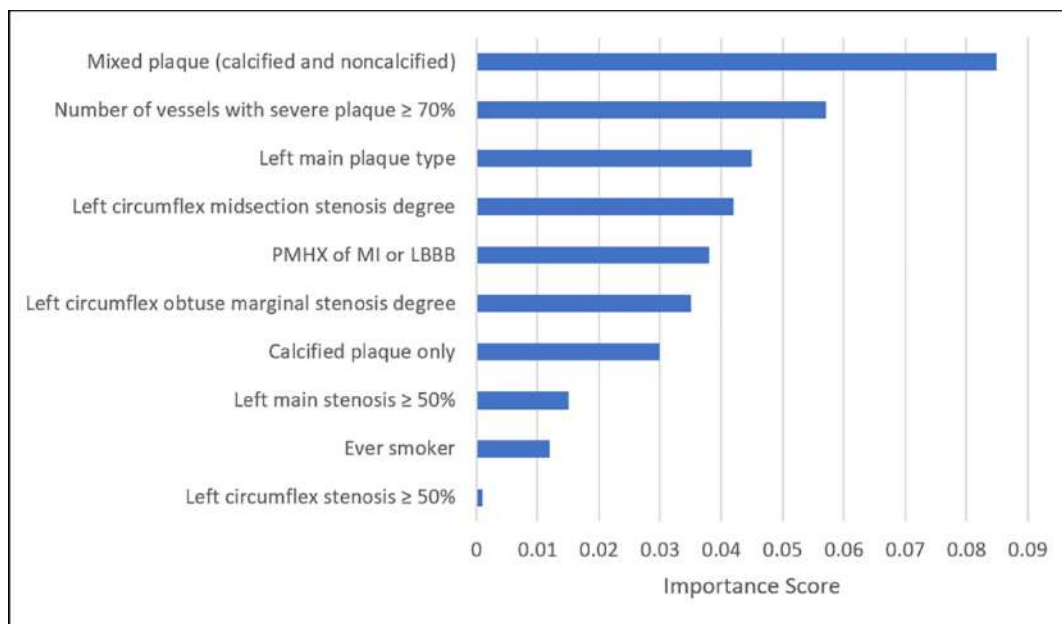
! Major adverse cardiac events (MACE)

- ✓ Composite machine learning (ML) risk scores were derived from imaging and clinical data which could be presented to physicians as an annualized event risk. 19% of patients with normal visual diagnosis (red arrow) were in the 95th percentile of MACE risk computed by ML
- ✓ Ref: Betancur et al, Prognostic Value of Combined Clinical and Myocardial Perfusion Imaging Data Using Machine Learning. JACC: Cardiovascular Imaging. 2018;11:1000-9



Feature importance ranking of the machine learning model for predictive MACE.

- ✓ Only the top 10 most important features were labelled

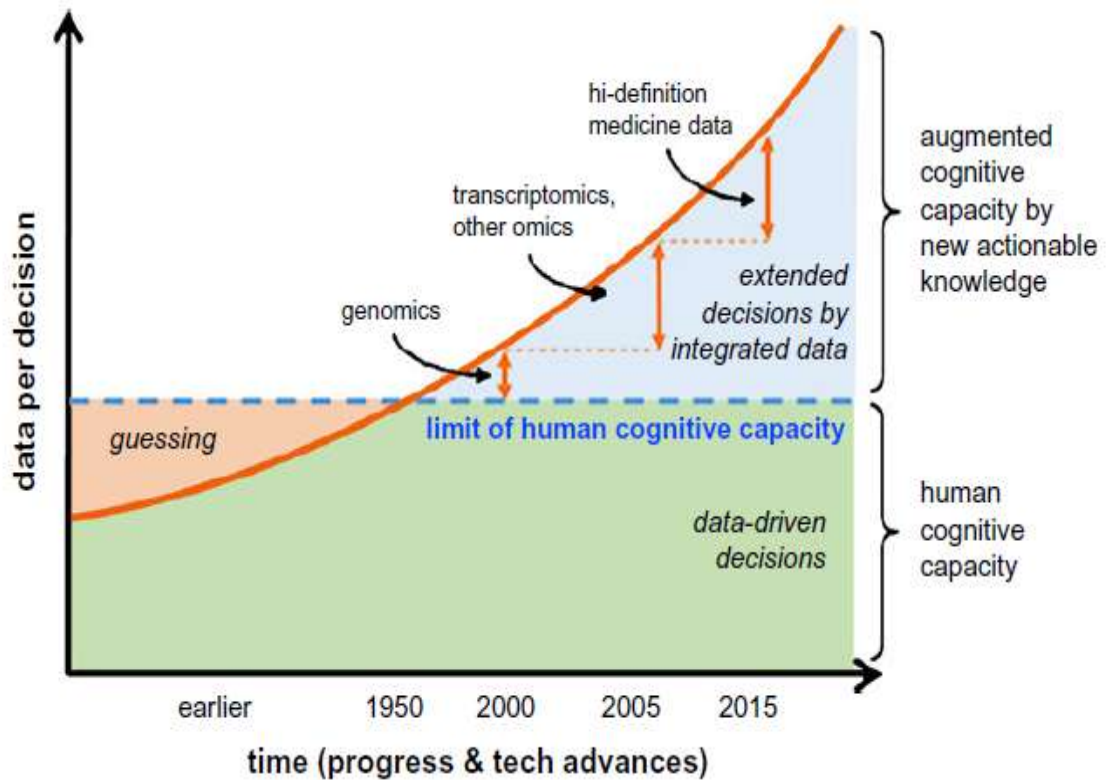


Permutation feature importance scores for the top ten features in the ensemble model for predicting MACE risk.



# Data Cardiology

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Escalating volumes of data are changing the decision-making process. The accelerated rate of data production, volume and variety now supersedes the limits of human cognitive capacity.

- ✓ Ref: Rossi RL, Grifantini RN. Big data: challenge and opportunity for translational and industrial research in healthcare. *Front Digit Humanit*; 2020

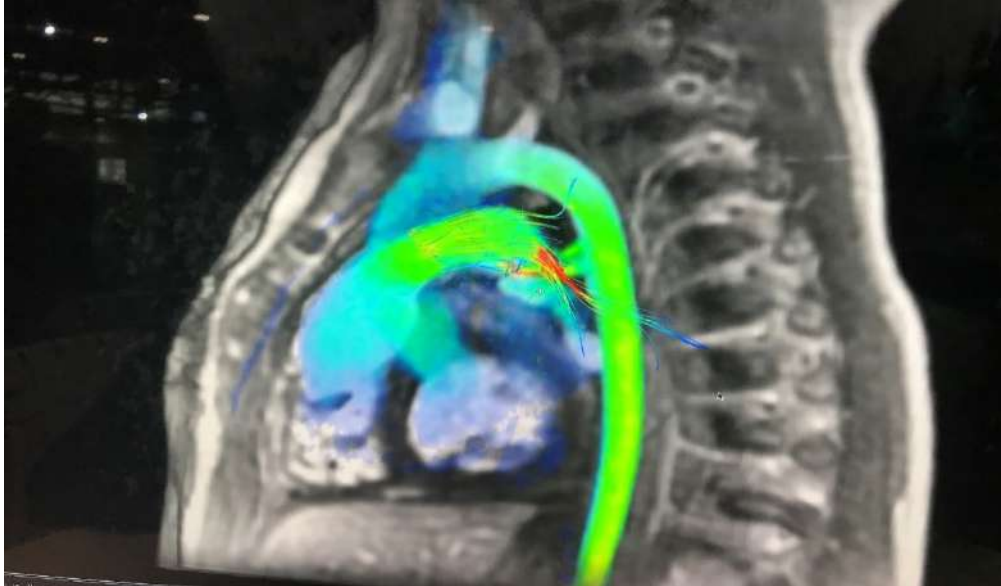
## Cardiac Instruments

AI +cardiology +Instrum

# MRI

## For Cardiology

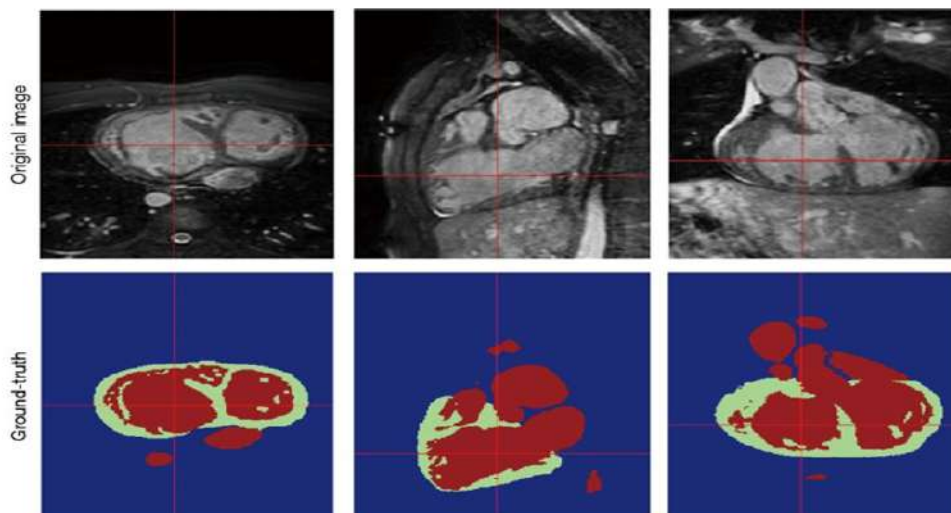
18



An example of cardiac MRI automated assessment software from Arterys

- + Shows dynamic blood flow and velocities and to perform auto quantifications.
- + Alg. now integrated into several MRI vendors' post-processing software

34

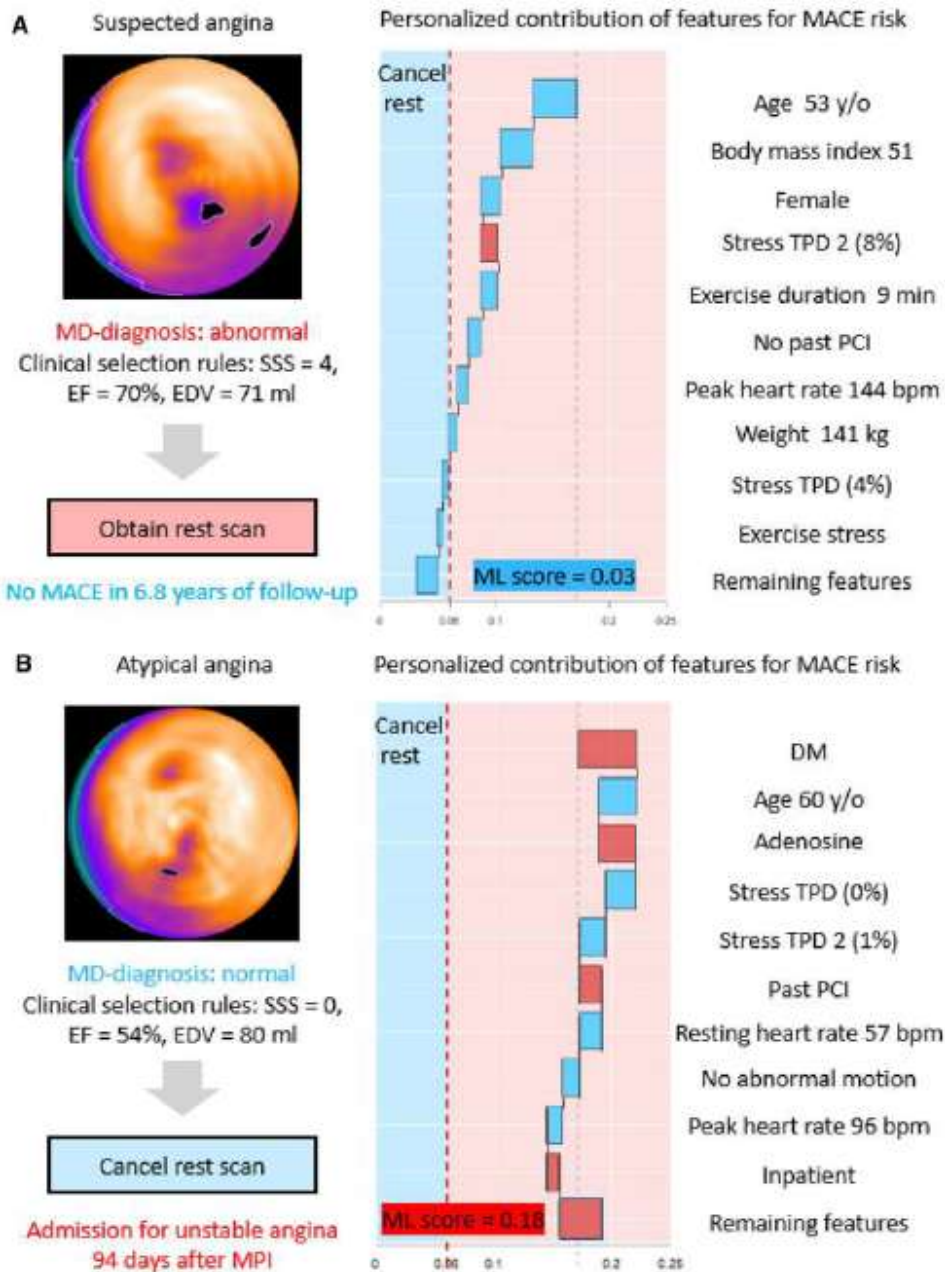


- ✓ A sample image of segmentation performed on cardiac MRI data from a patient with CHD.
- ✓ The myocardium is green and blood pool is red.

✓ From Arafati A, et al. Artificial intelligence in pediatric and adult congenital cardiac MRI: an unmet clinical need. *Cardiovasc Diag Ther* 2019;9:S310–25. Obtained with permission

# SPECT

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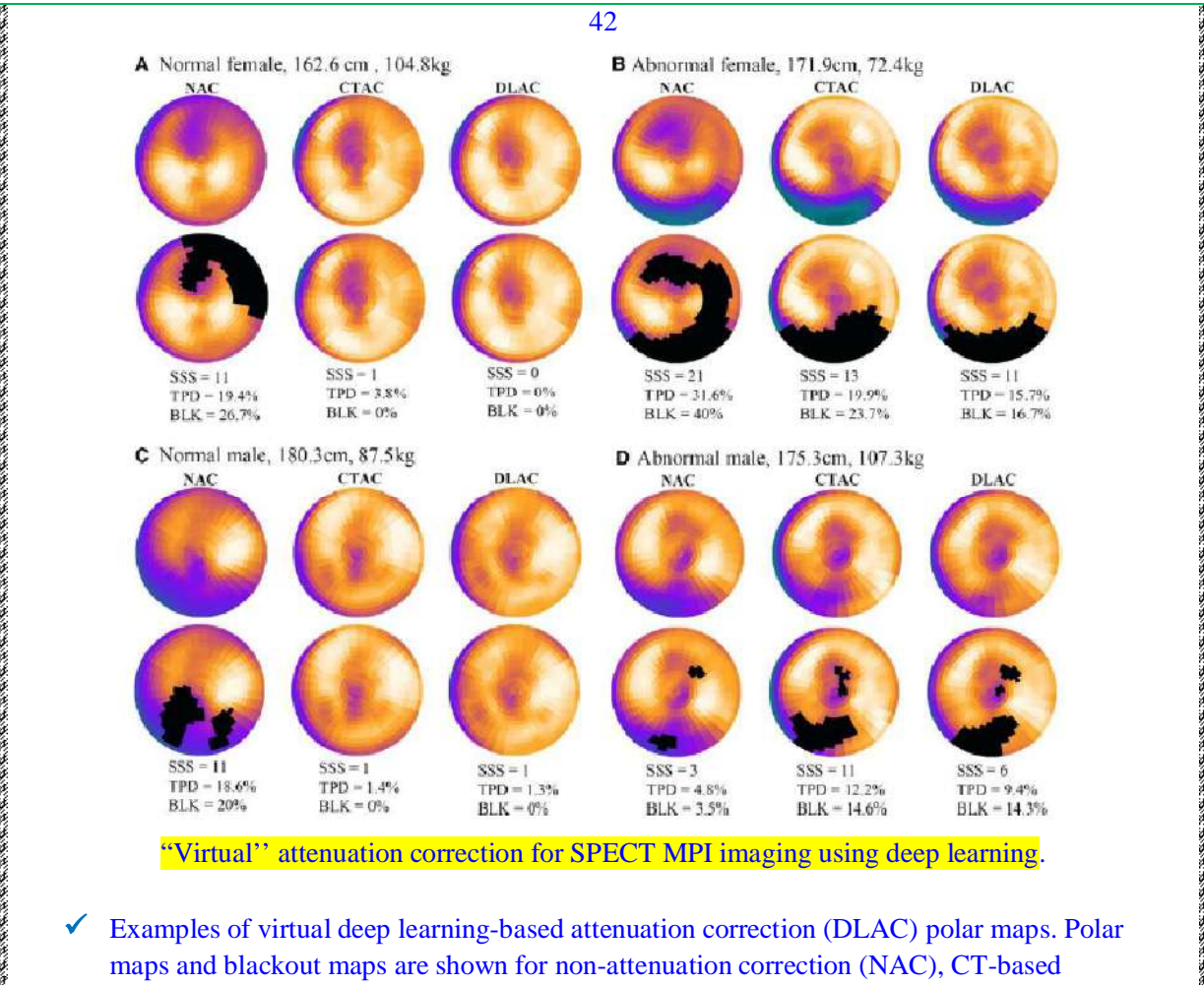


Machine learning prognosis-based safe-selection for stress-only SPECT.

- ✓ Polar maps with clinical recommendation (left) and
- ✓ personalized explanations of the ML recommendation (right) are shown in two cases:
- ✓ A :a case with a ML score below the score threshold to recommend cancelling the rest scan and
- ✓ B :a case with a ML score higher than the threshold. The individual contributions of the top 10 features to the overall risk for each patient are shown (blue bars = decreasing risk, red bars = increasing risk). Grey dotted line indicates baseline cohort risk. Red dotted line indicates risk threshold, matching stress cancellation rate for the stringent clinical criteria.
- ✓ Reprinted with permission: Hu LH et al Prognostically safe stress-only single-photon emission computed tomography myocardial perfusion imaging guided by machine learning: report from REFINE SPECT. Eur Heart J Cardiovasc Imaging. 2021 <https://doi.org/10.1093/ehjci/jeaa134.22>

# SPECT MPI

## Deep Lrn

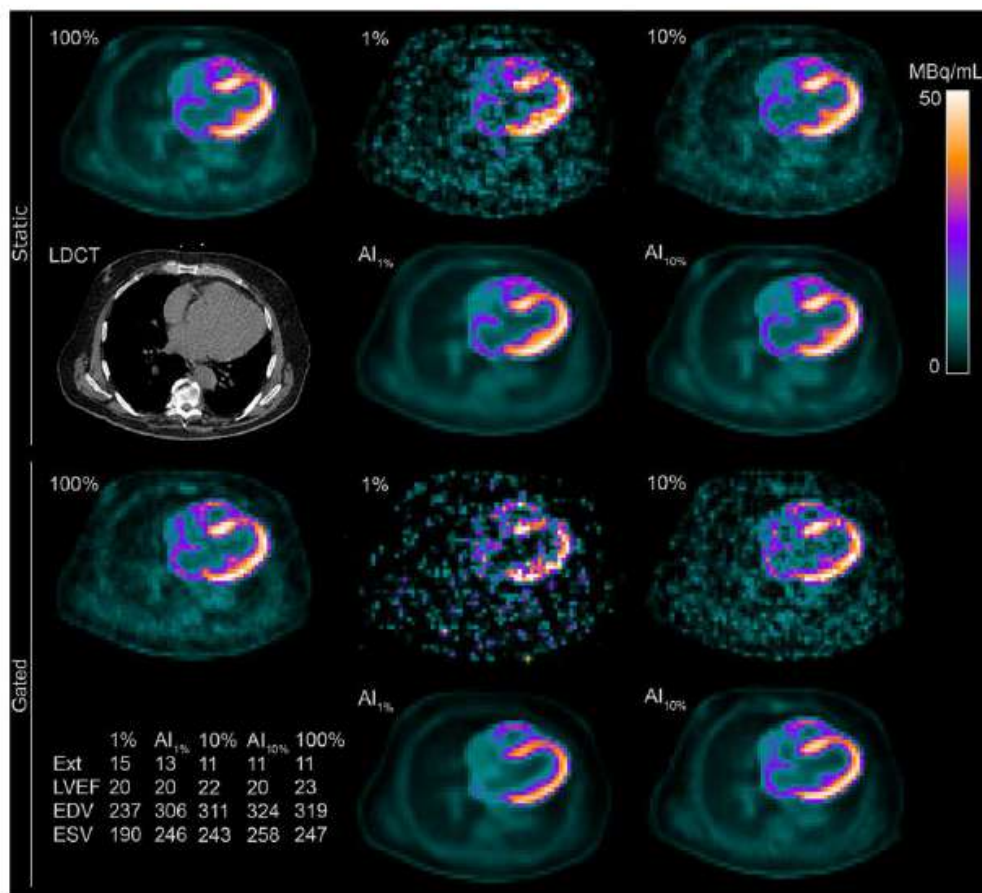


attenuation correction (CTAC), and

- ✓ DLAC for 4 patients: (A) normal female, (B) abnormal female, (C) normal male, and (D) abnormal male. SSS, TPD, and defect extent (BLK) are displayed for all polar maps.
- ✓ Ref: Hagio T, et al “Virtual” attenuation correction: improving stress myocardial perfusion SPECT imaging using deep learning. Eur J Nucl Med Mol Imaging. 2022 Mar 21. <https://doi.org/10.1007/s00259-022-05735->

## PET 18F-FDG

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Deep learning for noise reduction in low-dose FDG-PET imaging.

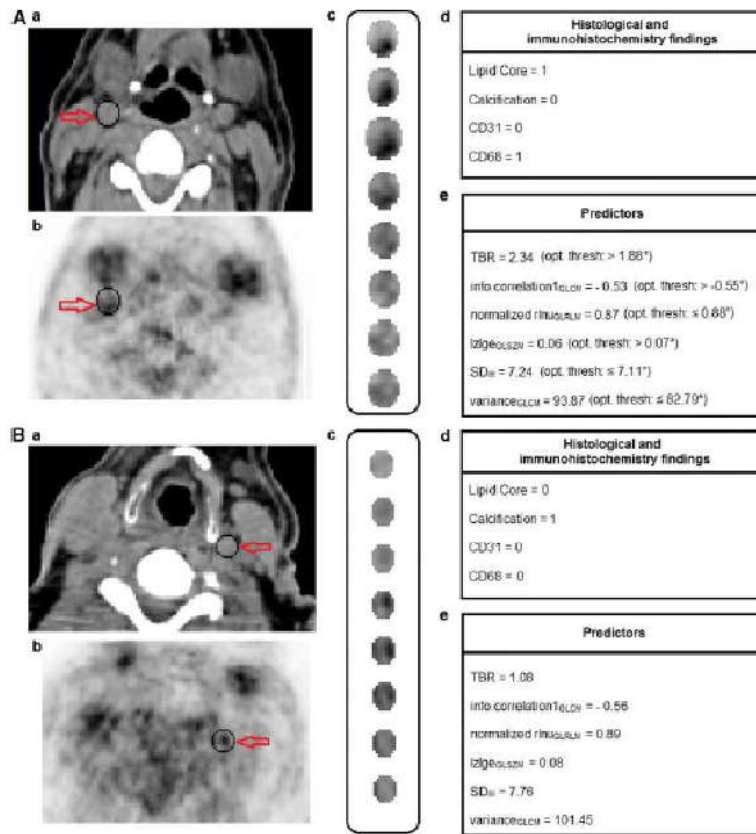
- ✓ Static (top two rows) and gated (bottom two rows). 18F-FDG PET images from a representative patient showing the effect of applying de-noising (AI<sub>1%</sub> and AI<sub>10%</sub>) to the low-dose images (1% and 10%). Low-dose CT (LDCT) shown for reference in mediastinum CT window. Extent (Ext),

LVEF, EDV, and ESV for the single subject are given for each dose-reduced image and the full-dose reference.

- ✓ Ref: Ladefoged CN, et al Low-dose PET image noise reduction using deep learning: application to cardiac viability FDG imaging in patients with ischemic heart disease. Phys Med Biol. 2021;66:054,003.24

## PET + CT Carotid plaque inflammation

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### Radiomic-based textural analysis for carotid plaque inflammation.

(A) CT (a) and PET(b) images of right carotid artery [black ROIs (red arrows)] in patient with high-grade stenosis and inflamed atherosclerotic plaque (extended lipid core and limited calcification), (c) Example ROIs manually placed around carotid artery wall on PET images, (d) Surgically derived histological and immunohistochemical analysis (CD31, cluster of differentiation 31; CD68, cluster of differentiation 68), (e) Corresponding values for target-to-background ratio (TBR) and textural features chosen for plaque vulnerability (opt. thresh, optimal threshold to detect increased histological and immunohistochemistry-based plaque characteristics; info.correlation1GLCM, first measure of information

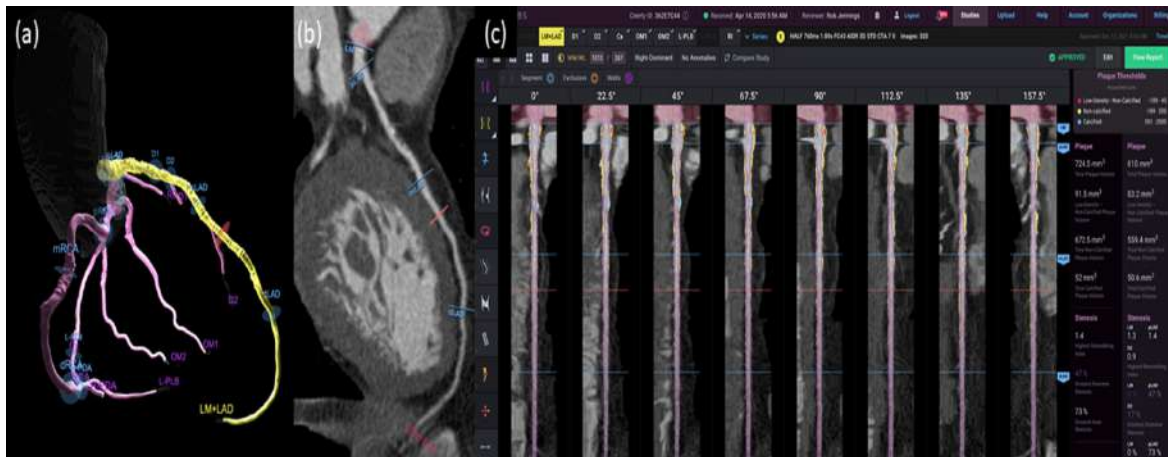
correlation; rlnuGLRLM, run length non-uniformity; lzlgGLSZM, large zone low gray level emphasis; SDIH, intensity histogram standard deviation, varianceGLCM, joint variance).

(B) one patient with left carotid artery atherosclerotic plaque with low inflammation (limited lipid core and extended calcification). Both cases demonstrate texture analysis can potentially provide valuable complementary information to TBR

Ref: Kafouris PP et al Fluorine-18fluorodeoxyglucose positron emission tomography-based textural features for prediction of event-prone carotid atherosclerotic plaques. J NuclCardiol. 2021;28:1861–1871

## Coronary CT angiogram

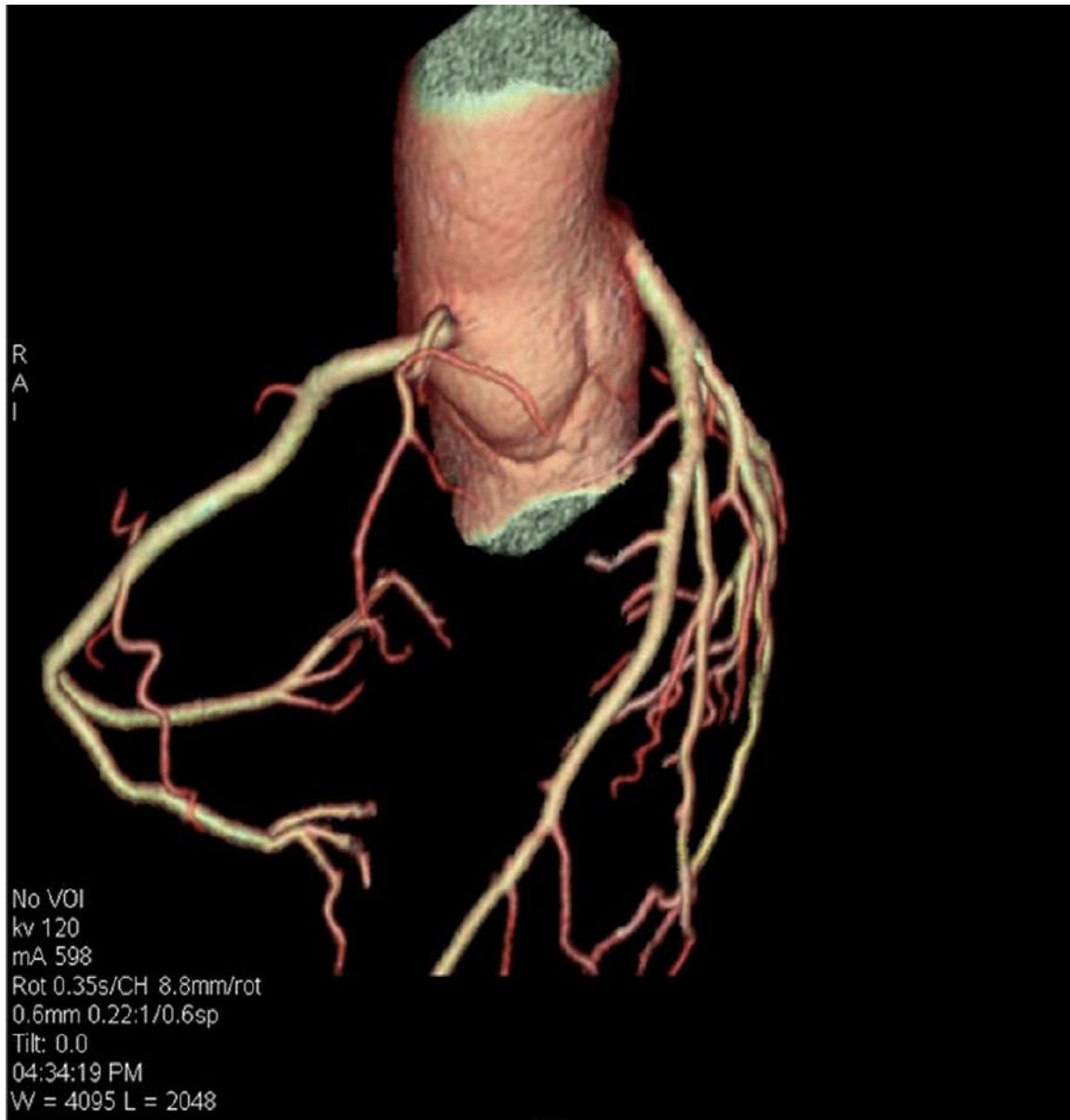
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Coronary CT angiogram of the left anterior descending artery (LAD)

- (a) topologically in volume rendered technique,
- (b) visually in curved multiplanar reformat, and
- (c) quantitatively in straightened multiplanar reformat across different 3D views.

This patient demonstrates high atherosclerotic plaque burden that is comprised primarily of non-calcified (yellow and red) rather than calcified plaque (blue). The ability to visualize both stenosis and plaque makes this modality unique among non-invasive imaging



**3D- volume rendered image of  
coronary arteries revealing largely normal vessels.**

- + The negative predictive power exceeds 99% for obstructive disease.

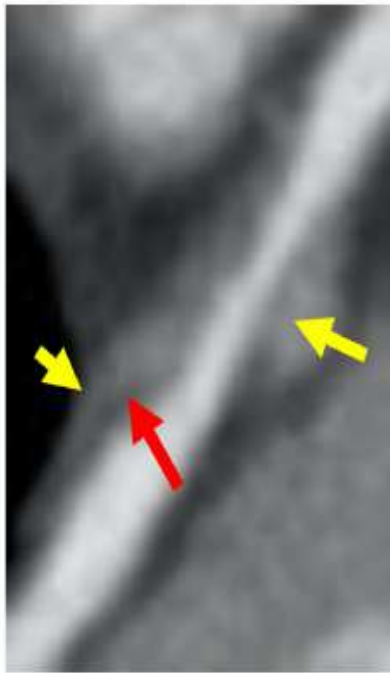




A 62 year old man with atypical chest pain.

- ✓ Computed tomographic angiography reveals severe atherosclerosis (mostly calcified plaque) without obstructive disease.
- ✓ The image demonstrates the ability to visualize the lumen clearly despite high calcium burdens

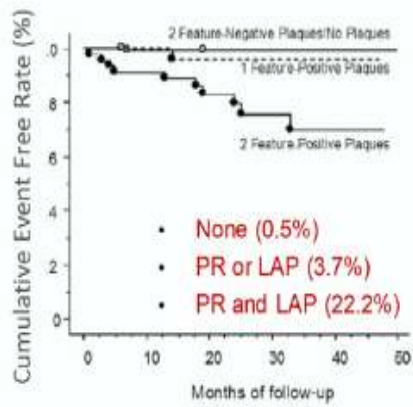
A1



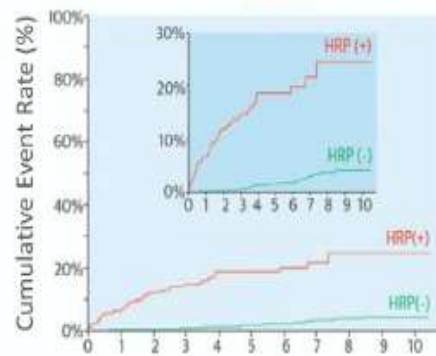
A2

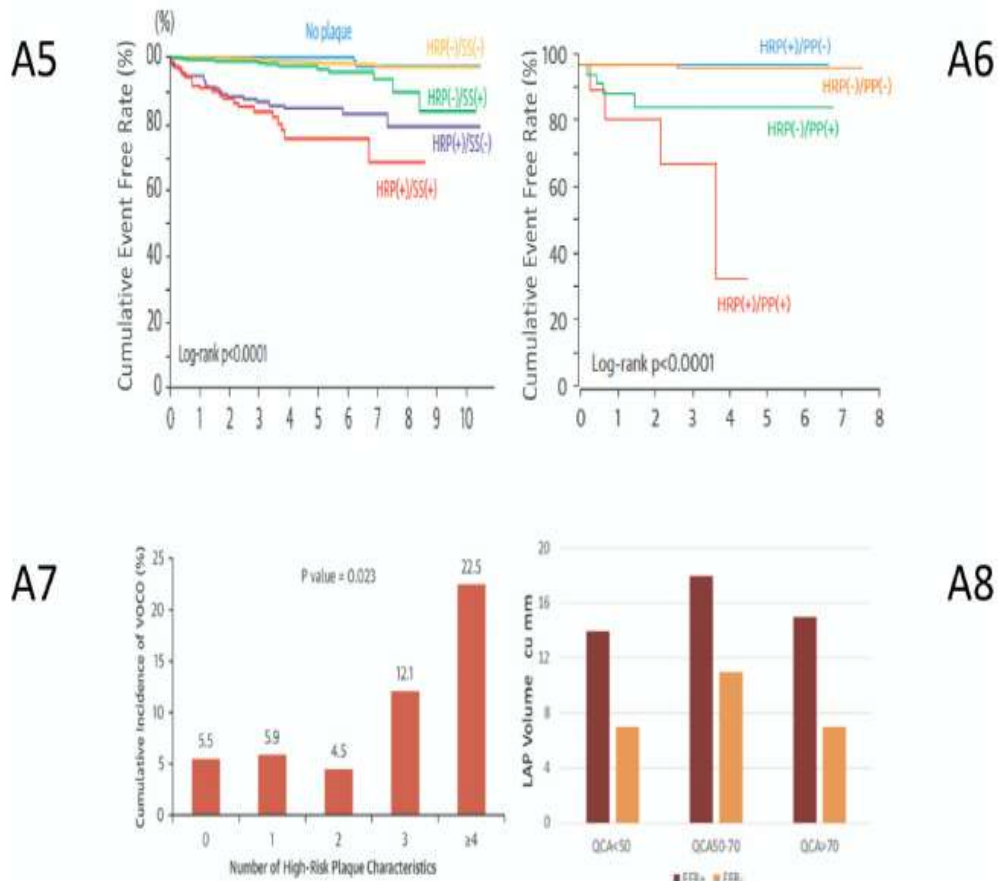


A3

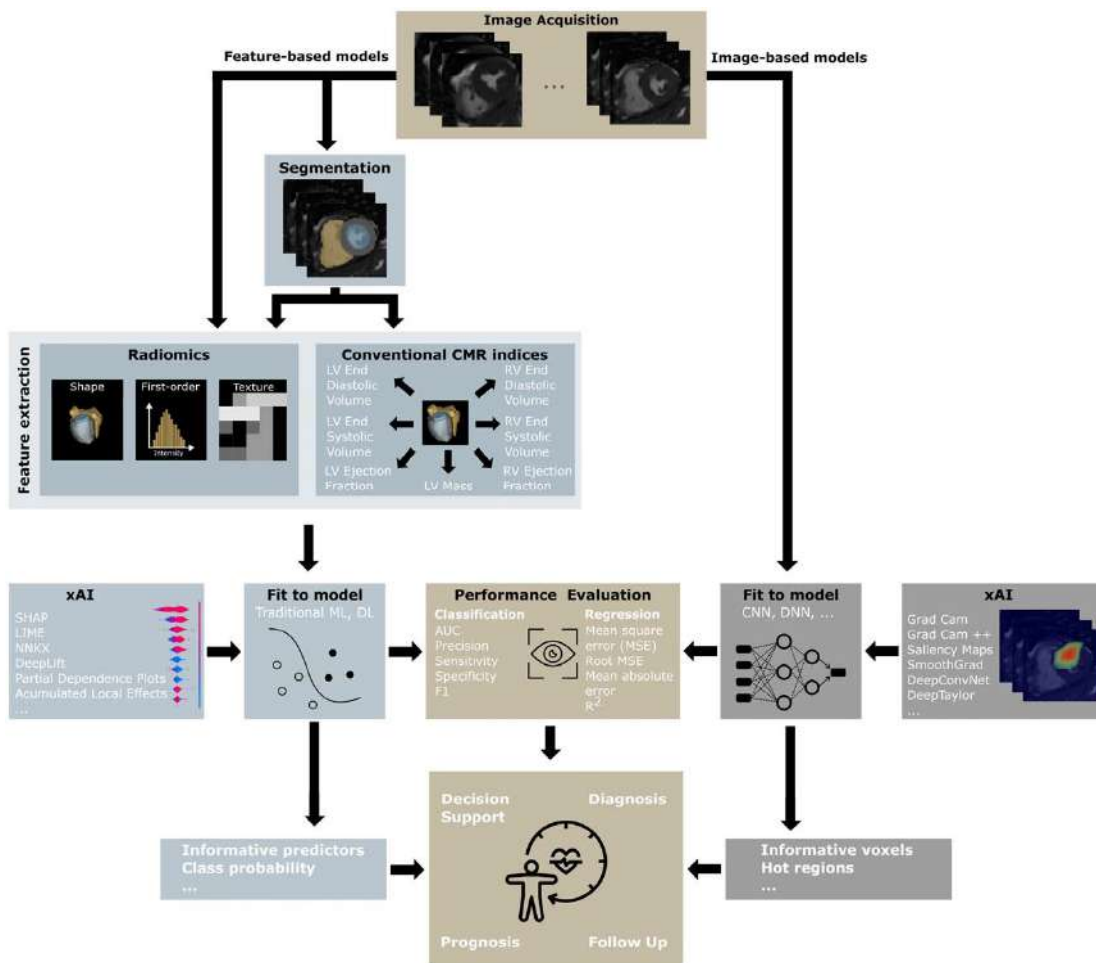


A4





Central Figure Legend: (A1) Presence of positive remodeling (yellow arrows) and low attenuation plaques (LAP, red arrow) are the most important determinants of plaque vulnerability. (A2) Stable plaques lack both these features. Major adverse cardiac events by the presence of 1 or both features in a follow up of —patients for 2 years (A3), and 300 patients for up to 10 years. (A4) Patients with HRP had 45 and 10 folds higher likelihood of adverse outcomes, respectively. Presence of obstructive disease over and above HRP features (A5) and interval progression in plaque magnitude (A6) increased the likelihood of adverse events further. Greater number of adverse plaque characteristics were associated with greater of adverse outcomes (A7) and the HRP characteristics were associated with abnormal fractional flow reserve regardless of luminal stenosis (A8). (Reprinted with permission of Elsevier )

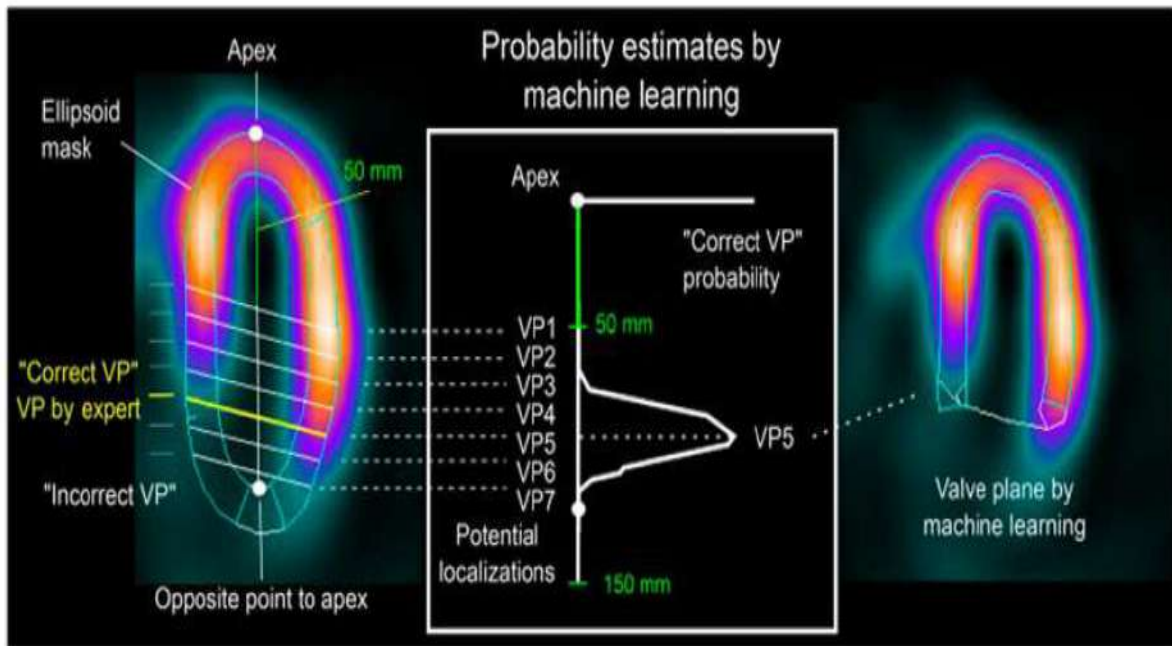


Overview of the 2 common paths that cardiac imaging studies might follow using cardiac magnetic resonance (CMR)

CNN, convolutional neural network; DeepConvNet, deep learning with CNN; DL, deep learning; DNN, deep neural network; NNKX, neural network knowledge extraction; XAI, explainable artificial intelligence; Grad-CAM, gradient-weighted class activation mapping; LIME, local interpretable model-agnostic explanations; SHAP, Shapley additive explanations; and LV, left ventricle; RV, right ventricle;

# Mitral valve

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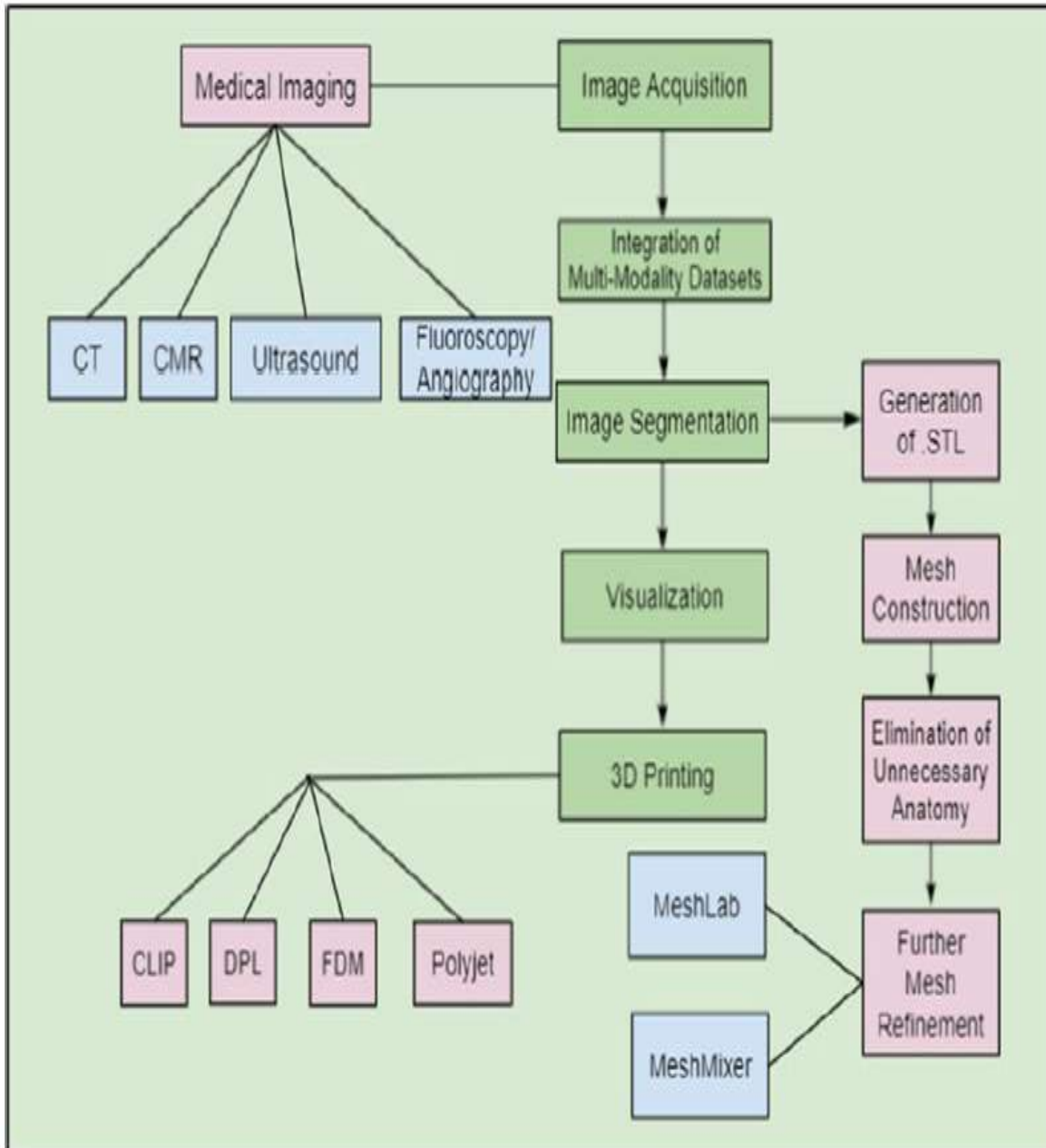


## Machine learning localization of mitral valve plane in MPI.

- ! A two-class support vector machine (SVM) model was trained from mitral valve plane (VP) positions verified by 2 experts to estimate the most likely VP localization in left ventricle.
  - o Ref: Betancur J et al Automatic valve plane localization in myocardial perfusion SPECT/CT by machine learning: anatomic and clinical validation. J Nucl Med. 2017;58:961–7.12

# 3D printing Cardiology

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Flowchart outlining the process of 3D printing in cardiology, from image acquisition to 3D printing.

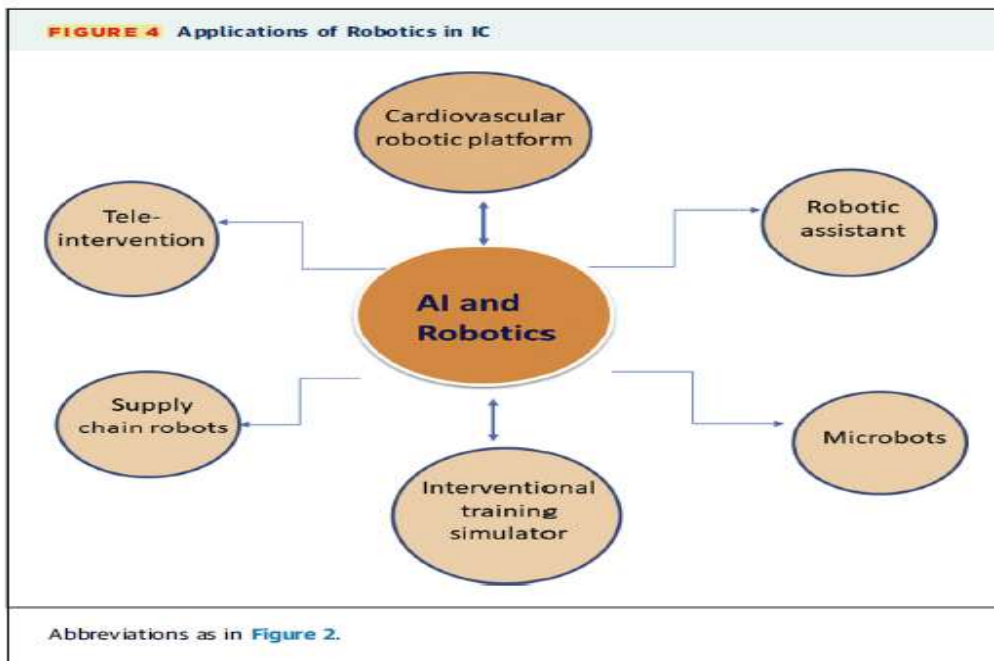
The chart also includes the software available for use.



Model of the heart and major arteries using a polyjet 3D printer

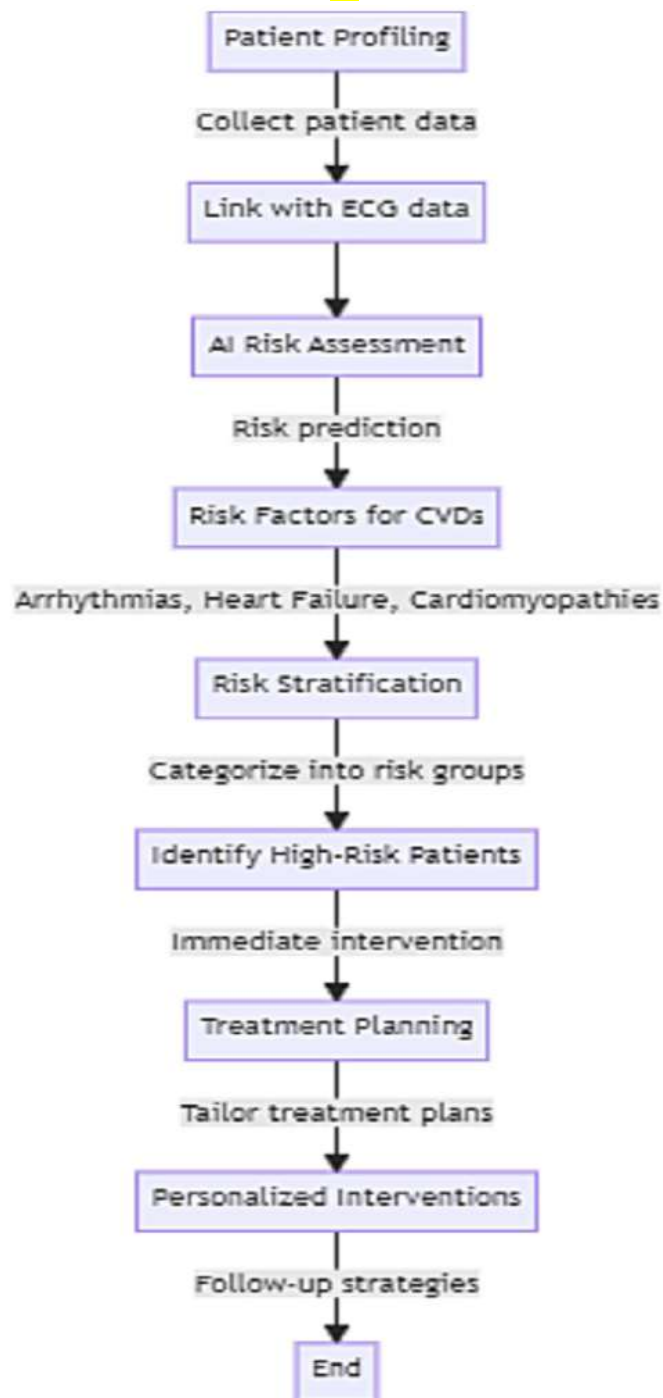
## Robotics

## Cardiology

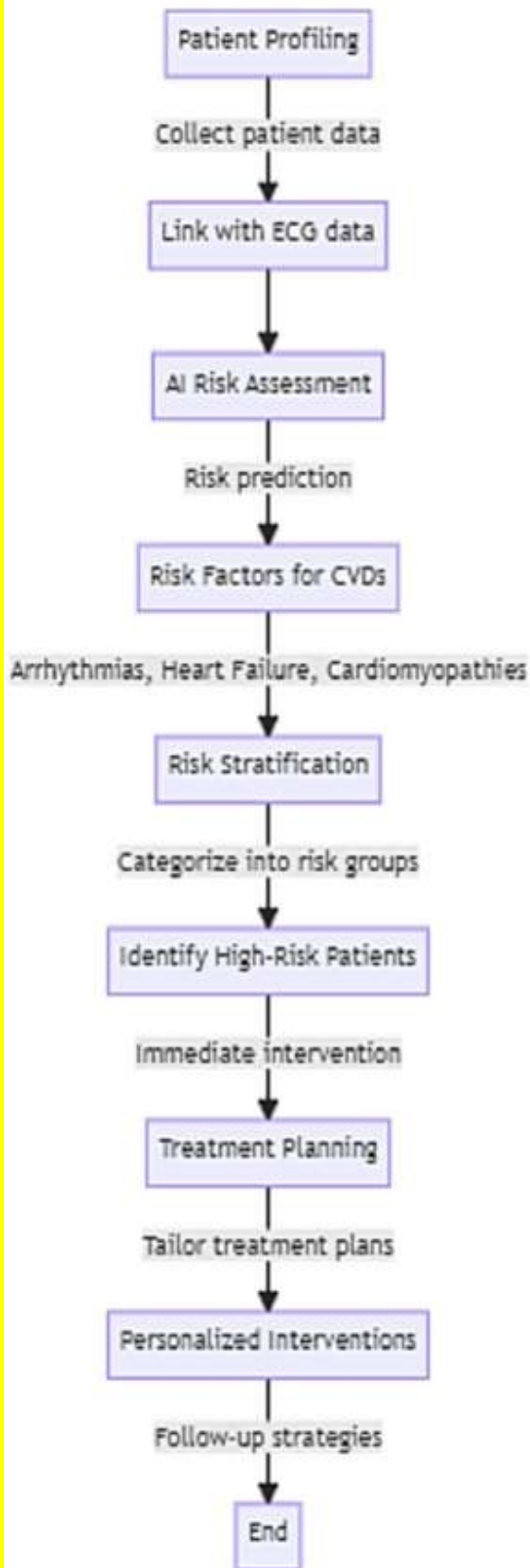


# Risk stratification AI + Cardiology

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AI enhance risk stratification for cardiovascular disease