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EKG

Emoke Posan

PartnerRe

AI-enabled EKG reading

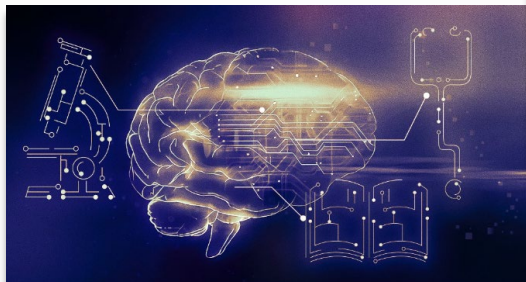
A NEW ERA

The Age of AI has begun

Artificial intelligence is as revolutionary as mobile phones and the Internet.

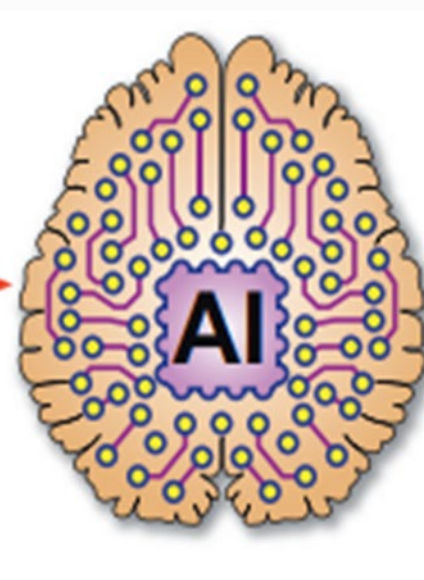
By **Bill Gates** | March 21, 2023 • 14 minute read

GatesNotes THE BLOG OF BILL GATES



"The development of AI is as fundamental as the creation of the microprocessor, the personal computer, the Internet, and the mobile phone [...] It will change the way people work, learn, travel, get health care, and communicate with each other."

-- Bill Gates

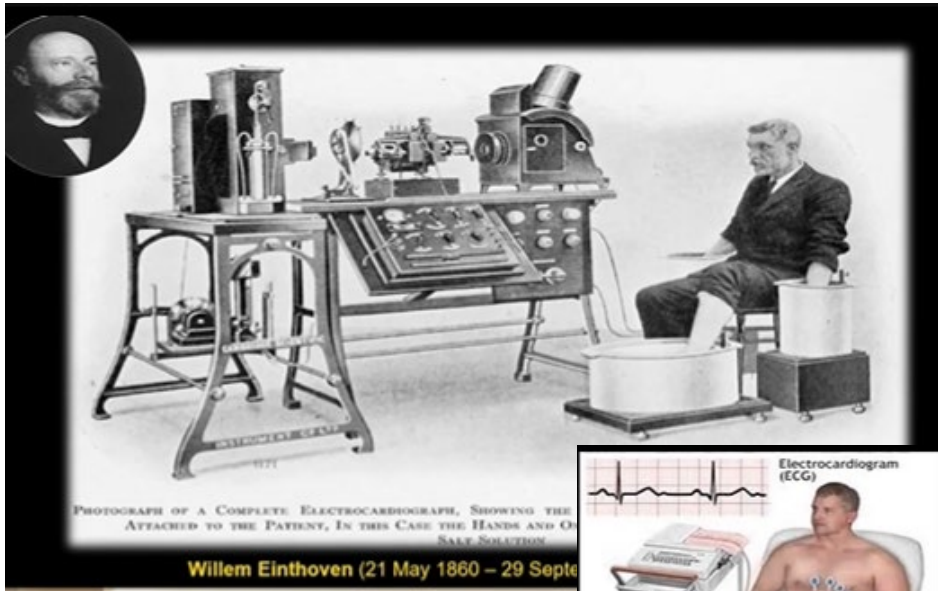


[Bill Gates Wants to Out-Plan the Next Pandemic - The Atlantic](#)
[The Age of AI has begun | Bill Gates \(gatesnotes.com\)](#)

Promise of AI-EKG

2023 – Washington, DC

Centenary of EKG Discovery

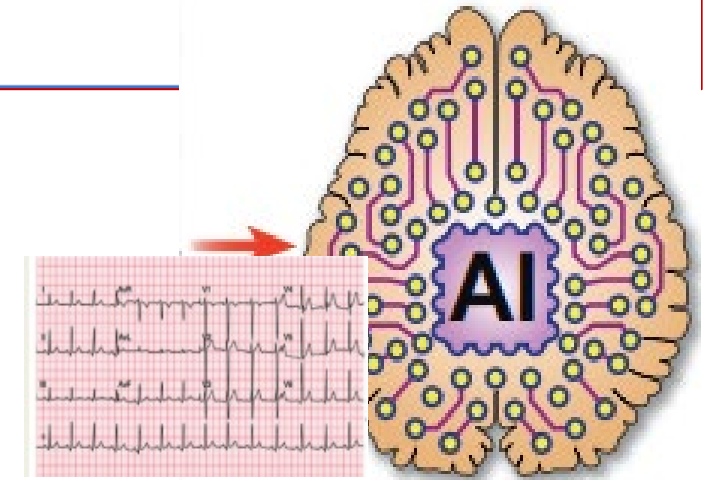


The Nobel Prize in Physiology or Medicine 1924



Photo from the Nobel Foundation archive.
Willem Einthoven

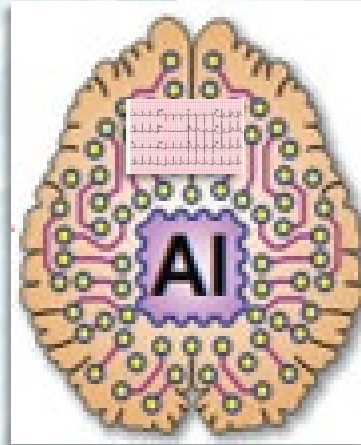
The Nobel Prize in Physiology or Medicine 1924 was awarded to Willem Einthoven "for his discovery of the mechanism of the electrocardiogram"



Unlocked Potentials in EKG innovation

AI-enabled EKG reading – “AI-EKG”

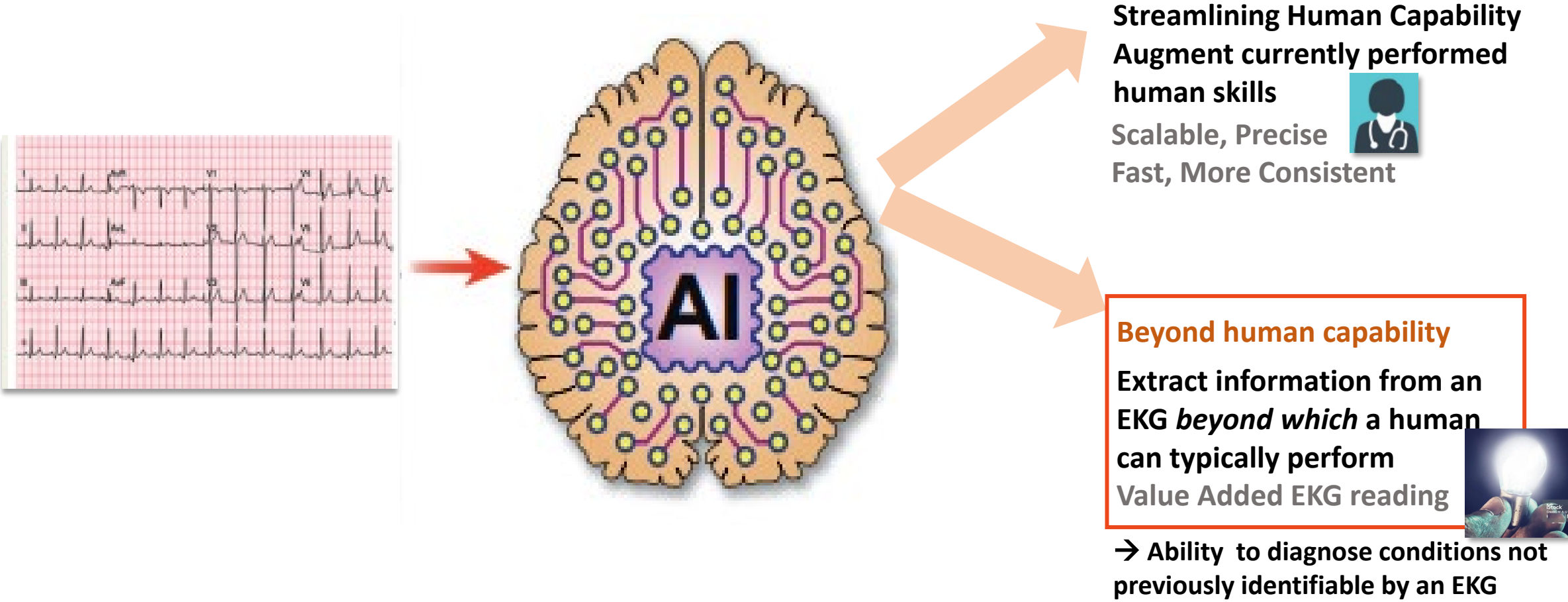
What is AI-EKG?



EKG reading Beyond human capacity

Extracting additional information

AI application to the EKG



Streamlining Human Capability
Augment currently performed human skills
Scalable, Precise
Fast, More Consistent



Beyond human capability
Extract information from an EKG *beyond which* a human can typically perform
Value Added EKG reading

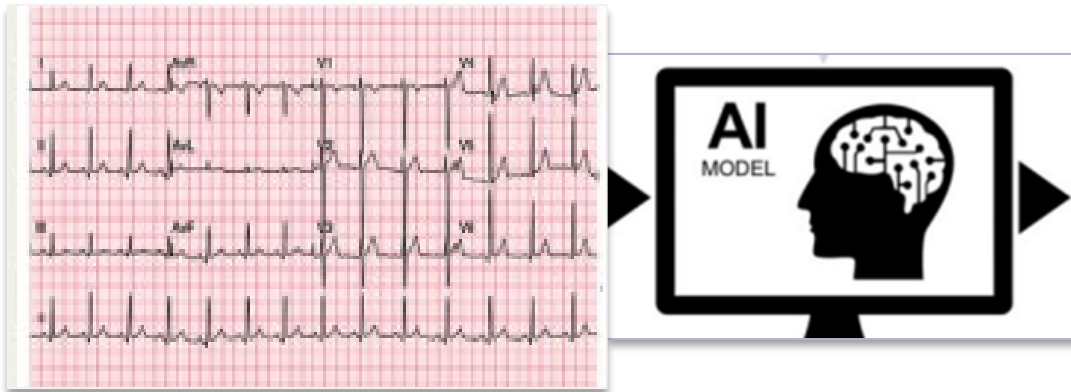


→ Ability to diagnose conditions not previously identifiable by an EKG

AI-EKG for enhanced diagnosis and prognosis – Deep Learning

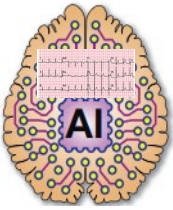
Future EKG reading

PROBABILISTIC INTERPRETATION vs 'normal/abnormal'

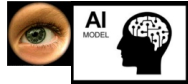


Estimated age:	39.5 years
Probability male:	99%
Estimated EF:	55%
Probability of low EF:	0.5%
Probability of undetected AF:	0.3%
Probability of HCM:	0.2%
Probability of aortic stenosis:	< 0.01%
Probability of cardiac amyloidosis:	0.03%

AGENDA:



➤ SEING BEYOND HUMAN INTERPRETATION



2 EXAMPLES - and 3 'detours'

- Background, Basic principles
- First Hypothesis testing, training and outcomes
- Performance of algorithm
- Case examples
- Clinical Utility- examples

- **± Case examples**
- **± Methodology insight**

- AREAS with Major development-
- Settings/form factors in which it can be used

➤ Overview

➤ Challenges **±**

➤ Summary/Conclusion

➤ Current status - Where are we at?

AI-EKG Background

Course of a Disease



I feel good!



SYMPTOMS AND SIGNS



Tests (time and cost)
diagnosis, treatment



Maybe LATE! First signs: MI, Stroke, SCD



Underlying physiological process starts many years earlier

Background

Course of a Disease



I feel good!

SYMPTOMS AND SIGNS



Tests (time and cost)
diagnosis, treatment



?LATE!

First signs: Stroke, MI, SCD

Silent –Asymptomatic LV dysfunction

6.5x risk clinical CHF, 1.6x risk death

Early diagnosis can mitigate the risk



~2%

Global population



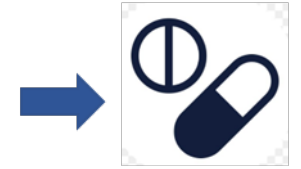
7M

Americans



~9%

>60y od



Treatments lower
mortality and HHF



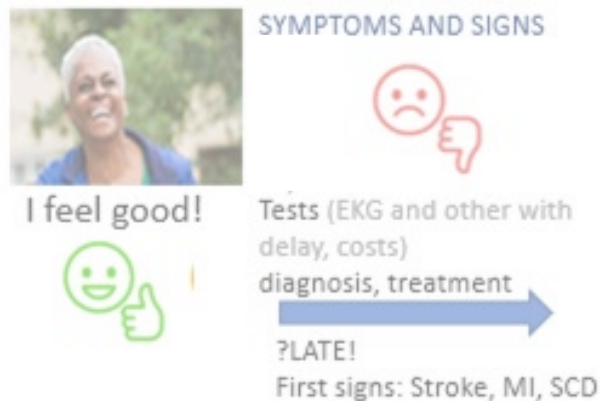
IDENTIFICATION REQUIRES EXPENSIVE,
NOT READILY AVAILABLE TESTS



NT-proBNP

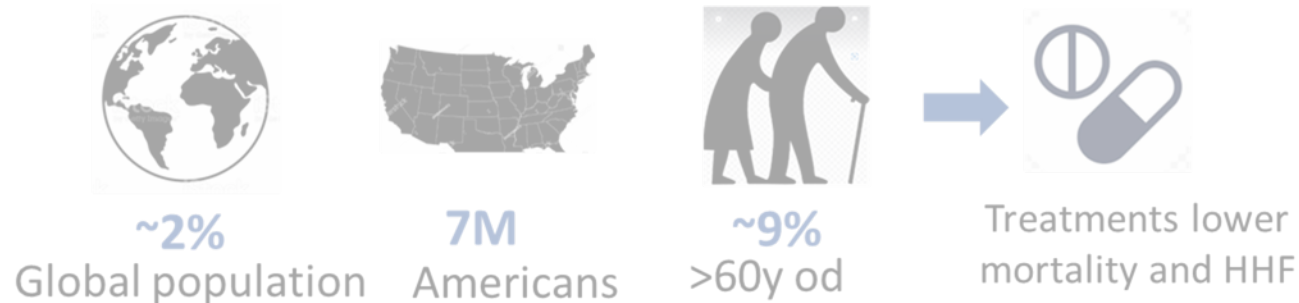
Background

Course of a Disease



Silent LV dysfunction

6.5x risk clinical CHF, 1.6x risk death



From Action Potential (AP) to EKG ... to all functions



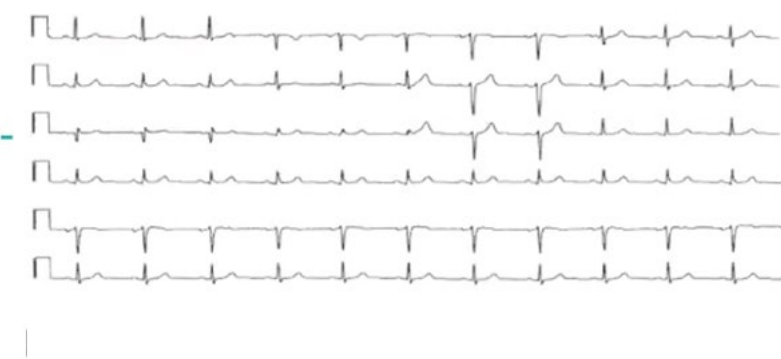
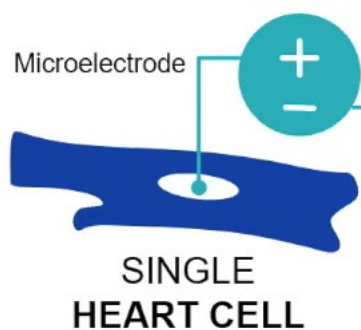
The EKG - cumulative recording at a distance (the body surface) of the AP of millions of individual cardiomyocytes

Background

Silent LV dysfunction

CURRENTS AND THEIR PROPAGATIONS ARE SENSITIVE TO CONDITIONS AND CHANGES

Disease process will initially affect the voltage (in time) before it manifests other ways

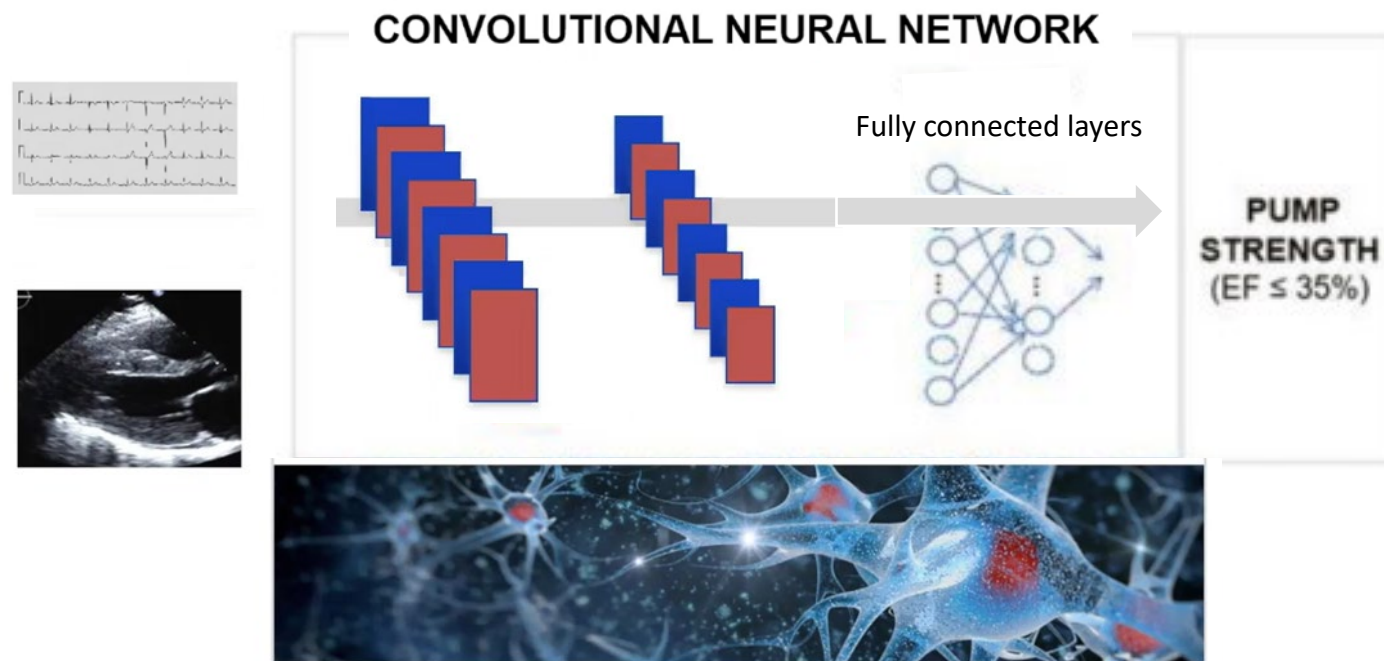


Application of artificial intelligence to the electrocardiogram, European Heart Journal (2021) 42, 4717–4730
Attia ZI. Screening for cardiac contractile dysfunction using an AI-enabled electrocardiogram. Nat Med. 2019 Jan;25(1):70-74. [Wearables, telemedicine and AI in arrhythmias \(escardio.org\)](https://www.nature.com/articles/s41591-018-0000-0)

HYPOTHESIS TESTING

Engineered and trained a network to recognize LVSD (DL)

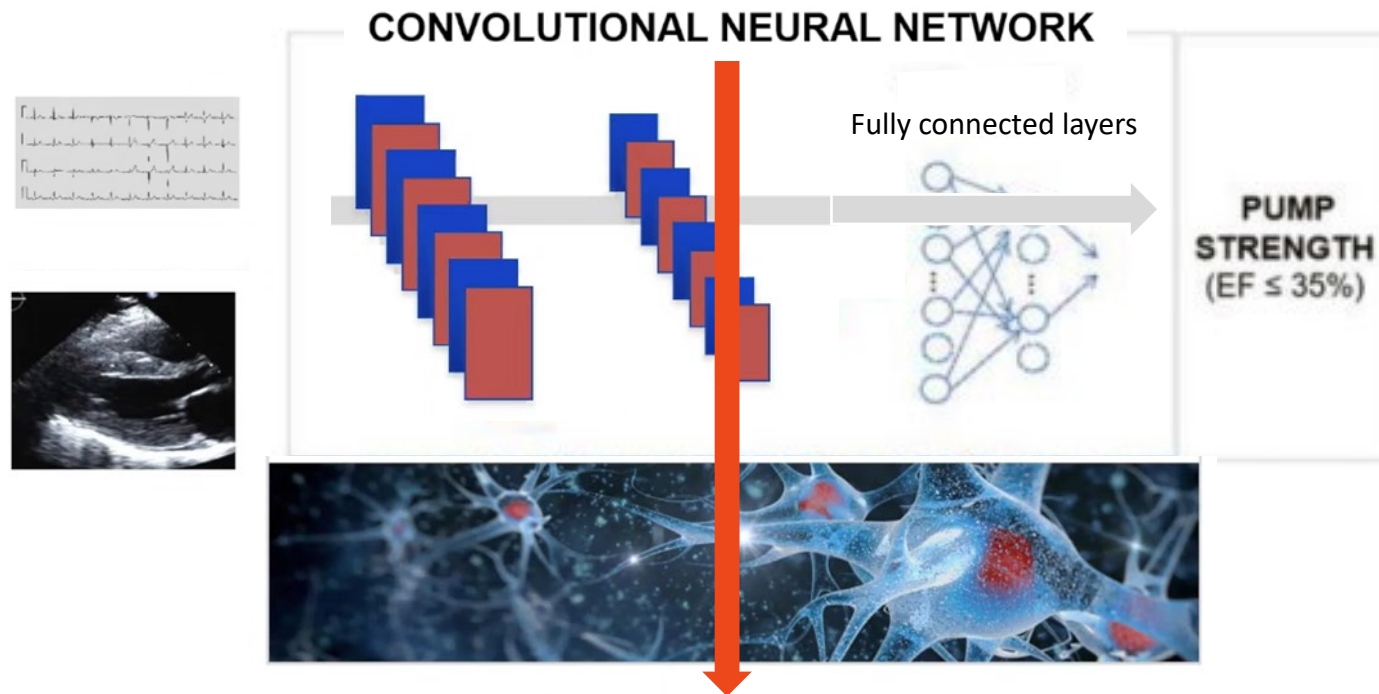
ROBUST DIGITAL WAREHOUSE OF MEDICAL INFORMATION



AI-EKG for enhanced diagnosis and prognosis - Deep Learning

HYPOTHESIS TESTING

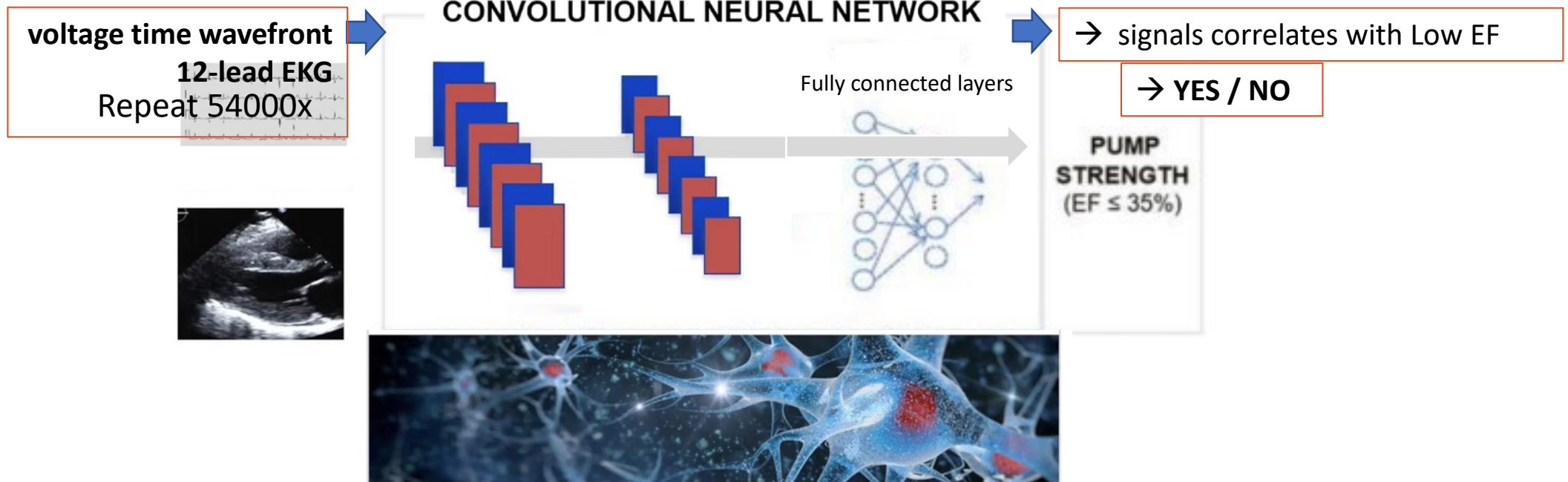
ROBUST DIGITAL WAREHOUSE OF MEDICAL INFORMATION



- to mimic/model human cortex
- each neuron is a mathematical formula
- Neurons are connected & Many layers-“deep”

HYPOTHESIS TESTING

I want to know if this EKG is Low EF or Not

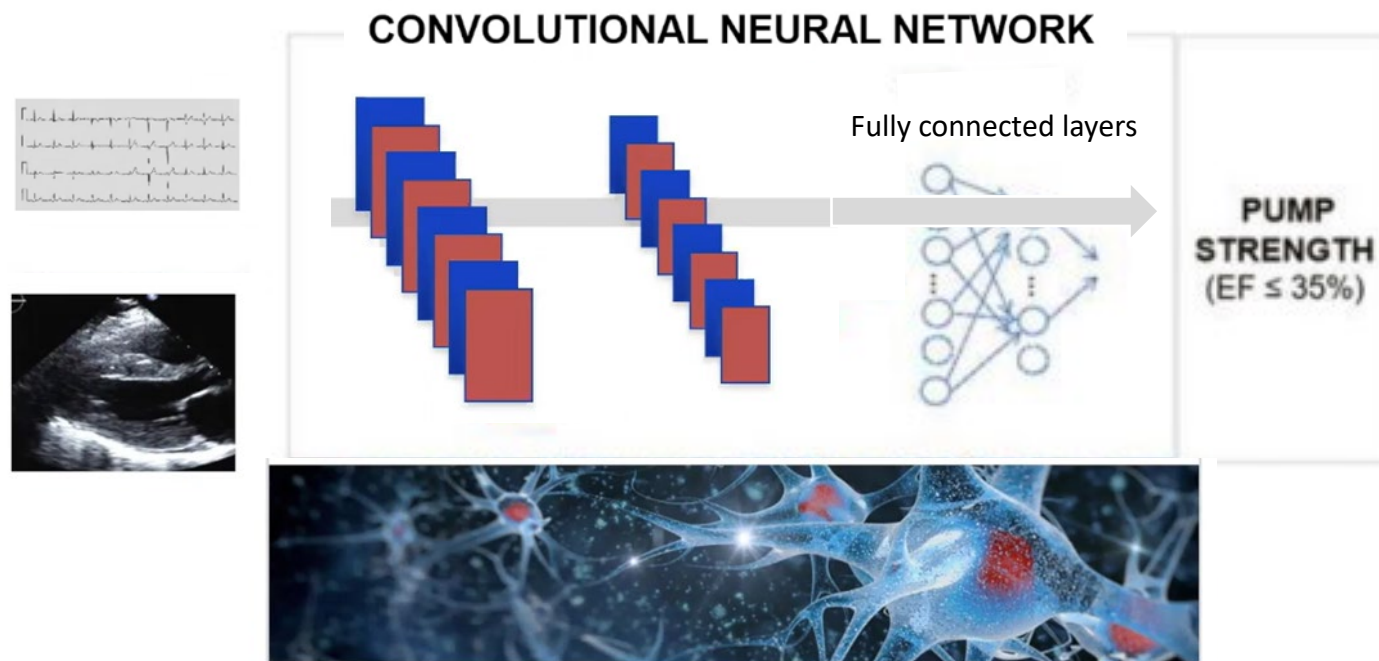


Large digital warehouse (600k pts- -98K paired EKG with echo) → 54k system **training**

HYPOTHESIS TESTING

DNN Trained (optimized) → Tested → Validated

- Training n= 36 000
- Testing ~9000
- Validation: ~53 000



Training: ← robust, large datasets, massive computer power

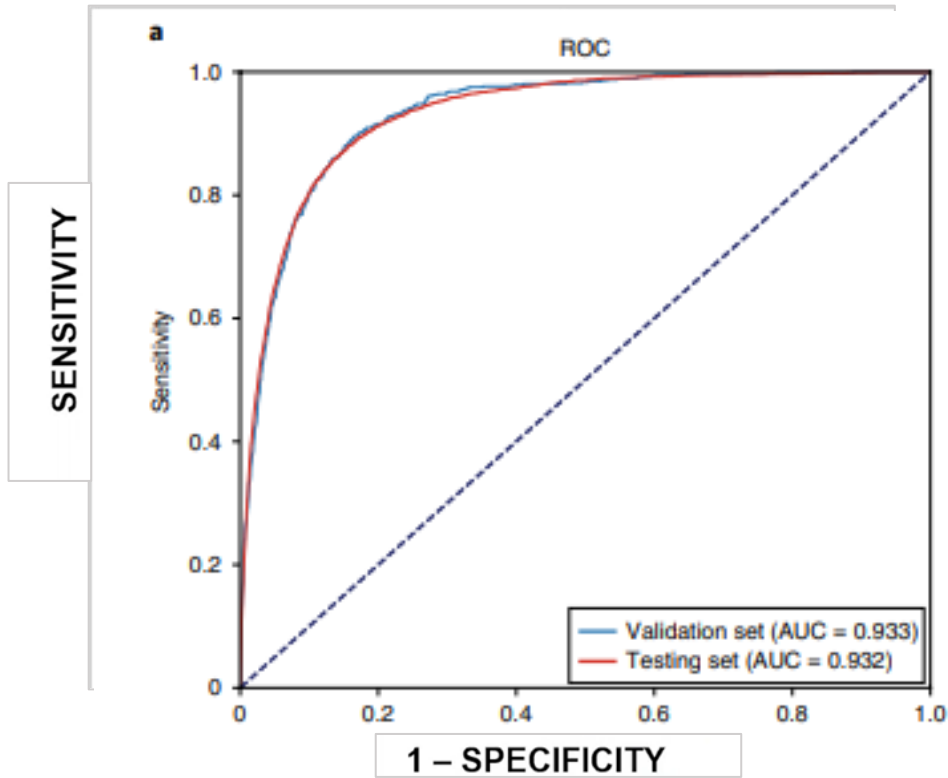
Once trained, it can be run on 12-lead, single lead

TESTING ← EKGs unknown to the network

Screening for cardiac contractile dysfunction using an AI-EKG

TEST PERFORMANCE

RECEIVER OPERATING CHARACTERISTICS



AREA UNDER THE CURVE OF EF

AUC – 0.93
PERFECT – 1.0



BNP and NT-proBNP -

To screen for systolic & diastolic dysfunction

NT-proBNP AUC 0.7-0.8

Treadmill test = 0.85

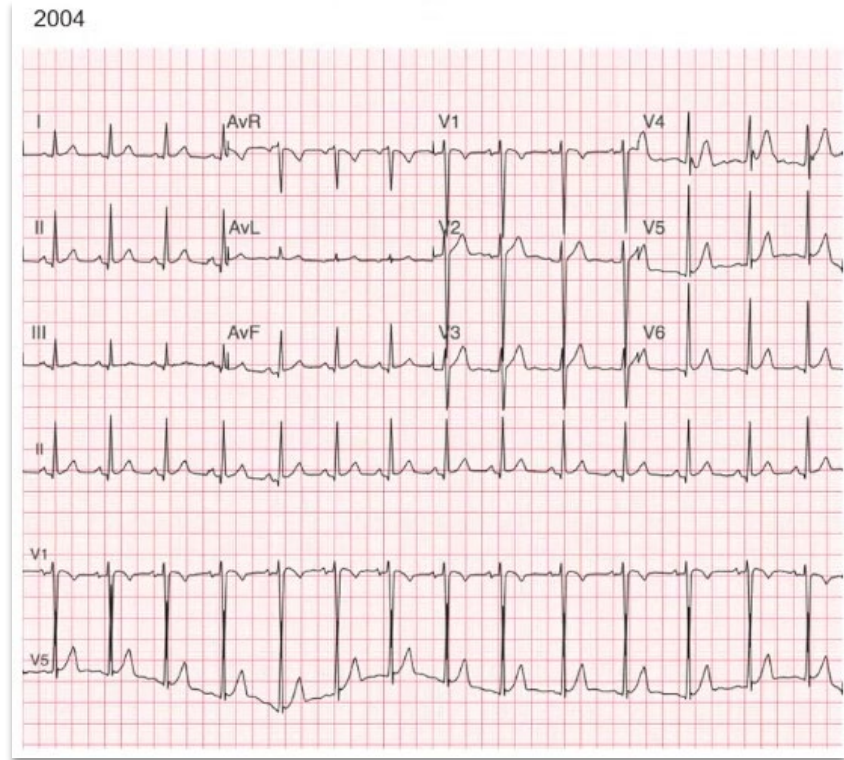
PAP Smear = 0.7

Mammogram = 0.85

1-Specificity Probability that a true negative will test positive. = FP

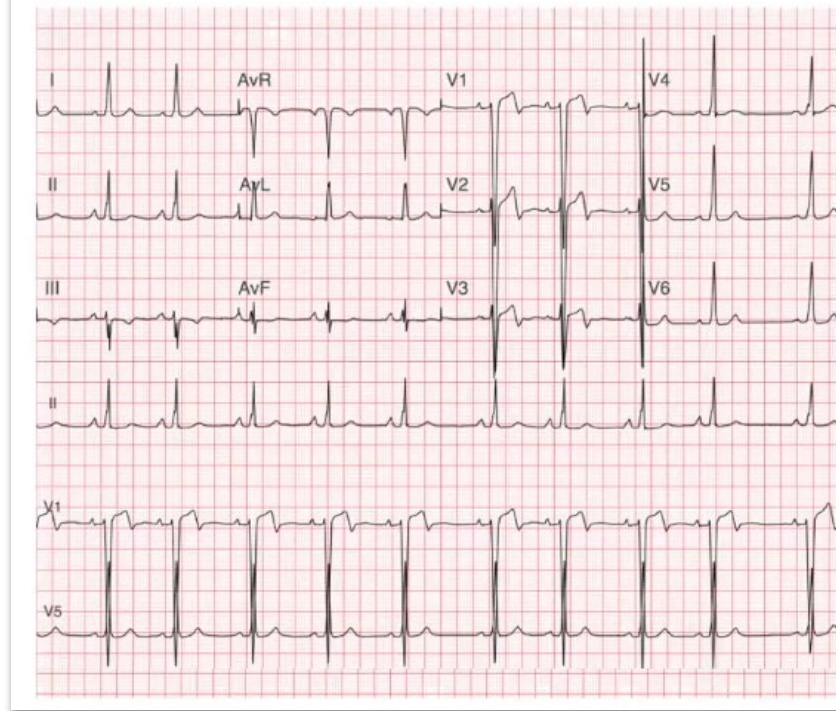
False positive for Low EF - EXAMPLE

AI EKG: positive for Low EF



Echo EF: 50%
False Positive

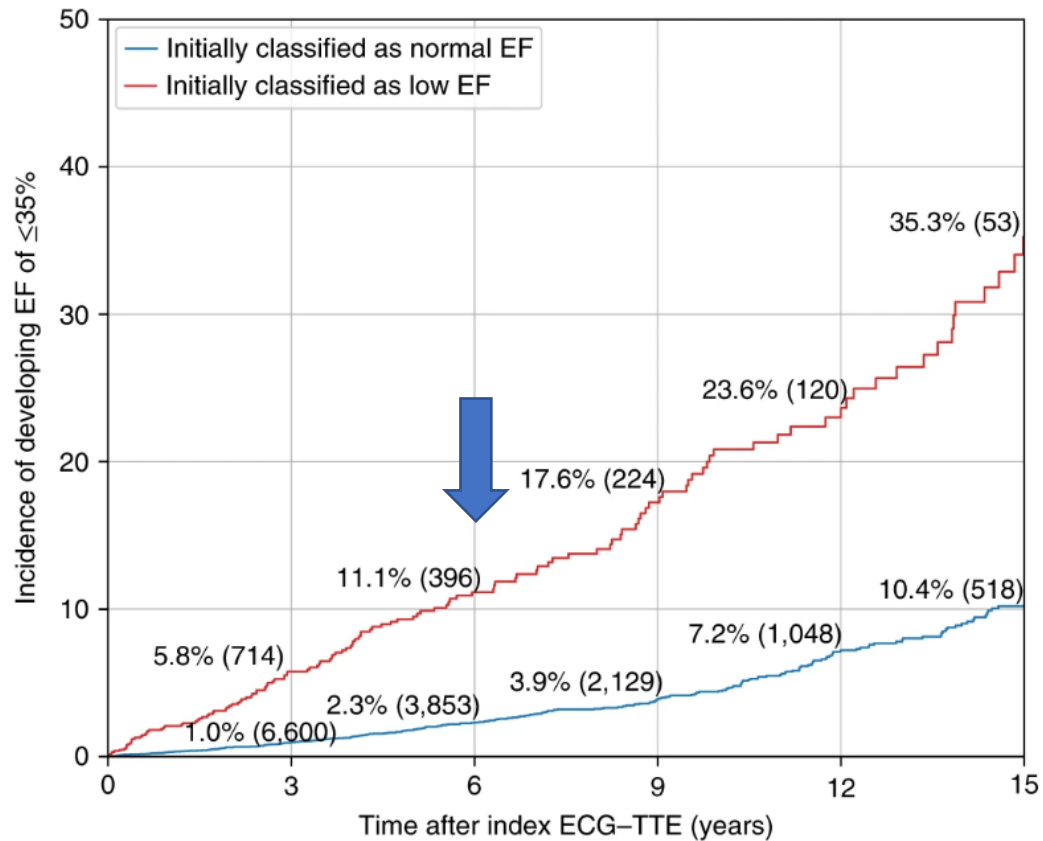
AI EKG: positive for Low EF
5 years later at age 33



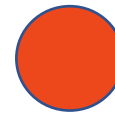
Echo EF: **31%**

LONG-TERM OUTCOME WITH A 'FALSE POSITIVE' - LOW EF AI- EKG

Long-term outcome of patients with an ECHO EF of $\geq 50\%$ at the time of initial classification Low-EF on AI-EKG



**INCIDENCE OF DEVELOPING LOW EF
OVER 6 YEAR – ~5X RISK**

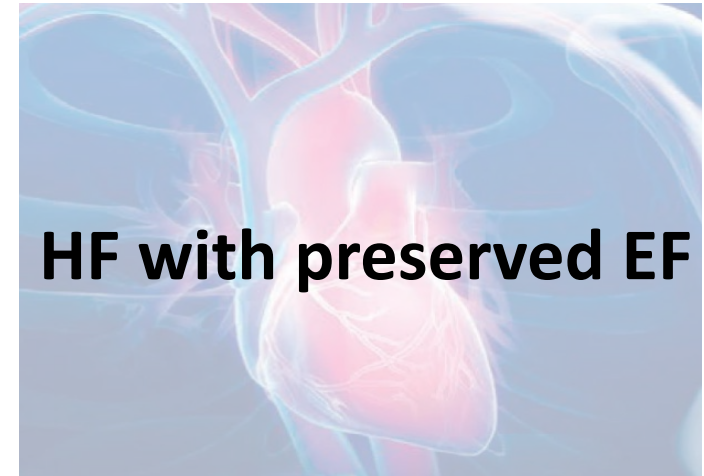


**PREDICT THE DISEASE -
before it becomes manifest**

→ Select pts to Arrange Imaging
Follow up in high risk groups 

AI disease 'previvor'

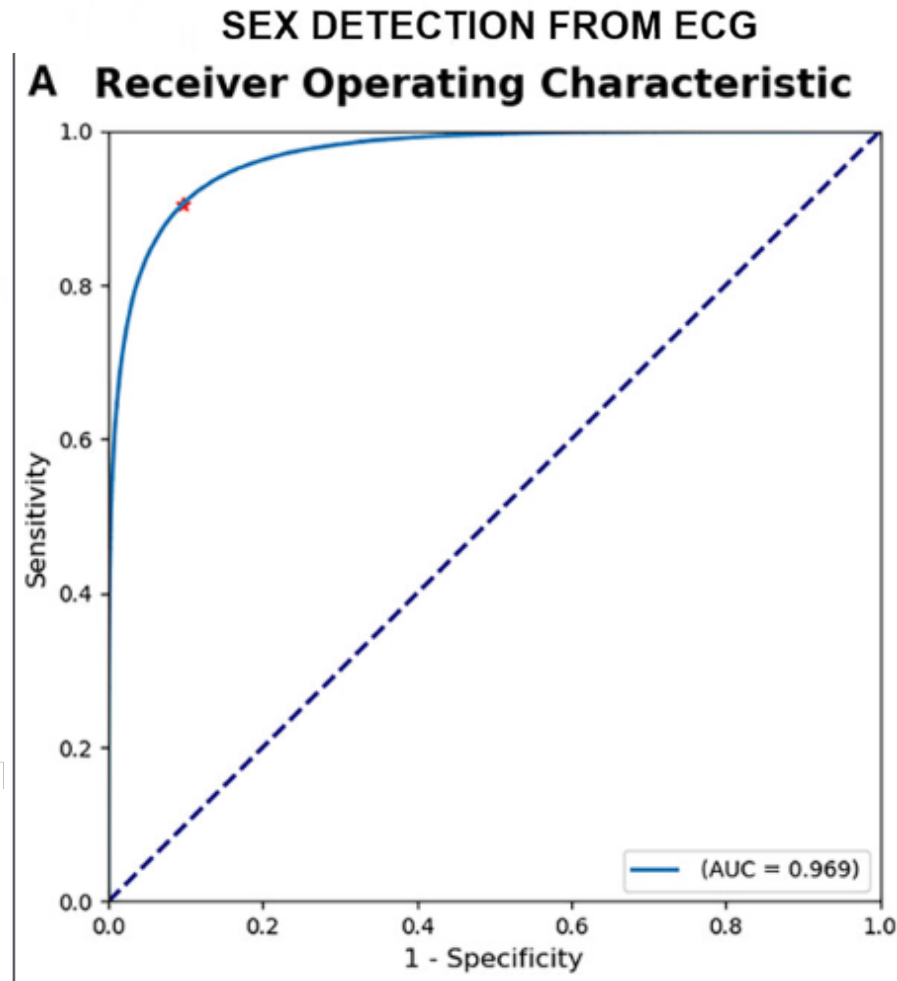
DETOUR - Major 'linked' developments



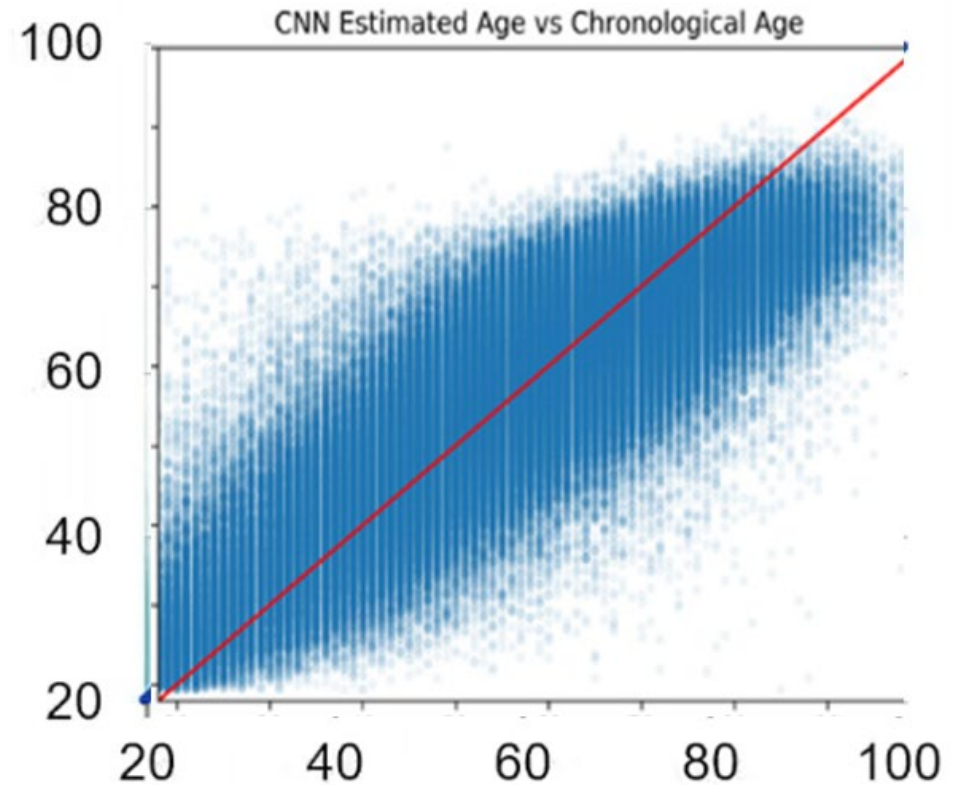
DETOUR - Major 'linked' developments



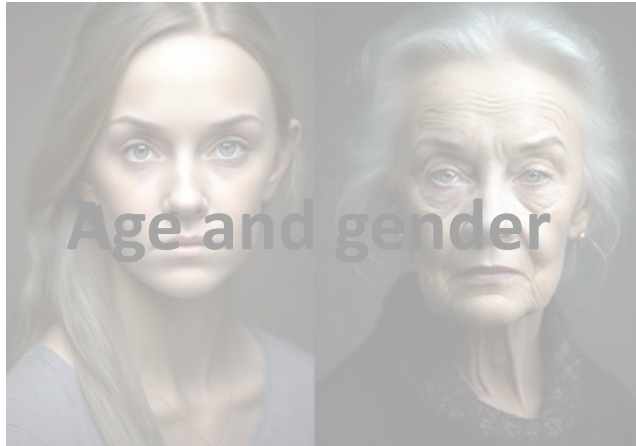
GENDER AND AGE FROM AI-EKG



**(CNN)-predicted age
vs reported age.**



DETOUR - Major 'linked' developments



CLINICAL UTILITY?
Consumer-grade wearable EKG



AI-EKG on APPLE WATCH – SINGLE LEAD LV SYSTOLIC DYSFUNCTION

Can a Watch Detect LV SYSTOLIC DYSFUNCTION? Mayo Apple WATCH study

nature medicine

Article

Prospective evaluation of smartwatch-enabled detection of left ventricular dysfunction

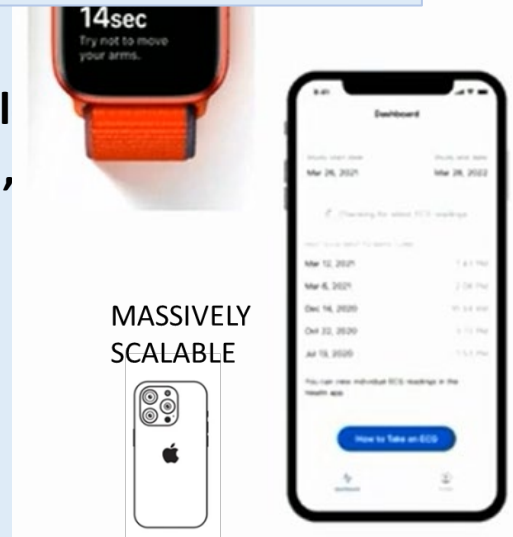
<https://doi.org/10.1038/s41591-022-02053-1>

Powerful test result – AUC 0.88
(vs AUC .93 on 12-lead)

Non-clinical environment! 12 → 1 lead

Major messages:

- 12-lead model can be modified and extrapolated to single lead
- Potential to diagnose disease from ‘anywhere’: ‘uniform’
 - Massive scalable tech for screening, dx, monitoring
 - New dimensions of Trials



Artificial intelligence

Smartwatch detection of left ventricular dysfunction

Artificial intelligence (AI) algorithms applied to electrocardiograms (ECGs) recorded by smartwatches can identify individuals with left ventricular dysfunction, according to a study published in *Nature Medicine*. “There is a huge need for



npj | digital medicine

Yale University

www.nature.com/npjdigitalmed

ARTICLE OPEN

Detection of left ventricular systolic dysfunction from single-lead electrocardiography adapted for portable and wearable devices

Akhay Khunte¹, Veer Sangha¹, Evangelos K. Oikonomou², Lovedeep S. Dhingra³, Arya Aminorroaya², Bobak J. Mortazavi⁴, Andreas Coppi⁵, Cynthia A. Brandt⁶, Harlan M. Krumholz^{7,8} and Rohan Kherra^{4,6,9}

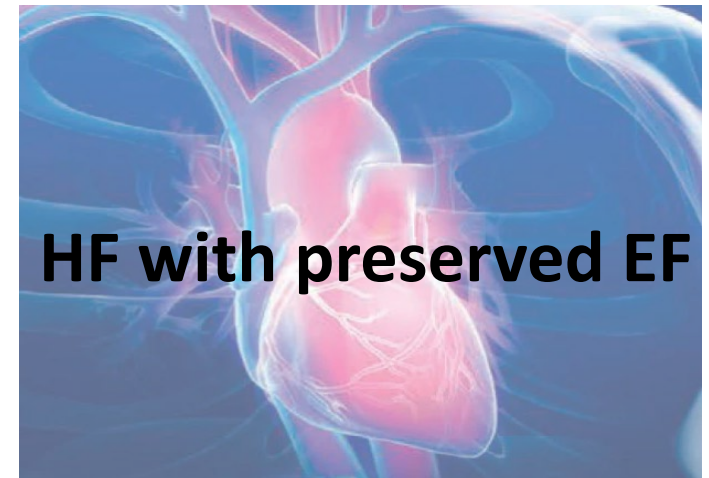
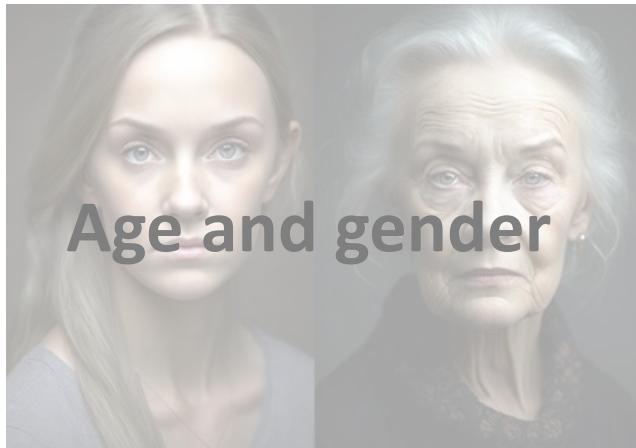
Nat. Med. 2022
doi.org/10.1038/s41591-022-02053-1

ECG
FROM
consumer
watch ECG
recordings



New App for Apple Watch Uses Artificial Intelligence to Detect Left-Ventricular Dysfunction

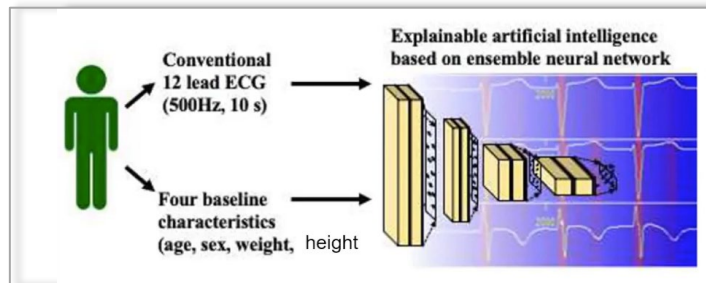
Major 'linked' developments



AI-EKG for HFpEF

Artificial intelligence assessment for early detection of heart failure with preserved ejection fraction based on electrocardiographic features

Joon-myung Kwon^{1,2,3,4}, Kyung-Hee Kim^{2,5*}, Howard J. Eisen⁶, Younghoon Cho⁴, Ki-Hyun Jeon^{2,5}, Soo Youn Lee^{2,5}, Jinsik Park⁵, and Byung-Hee Oh⁵



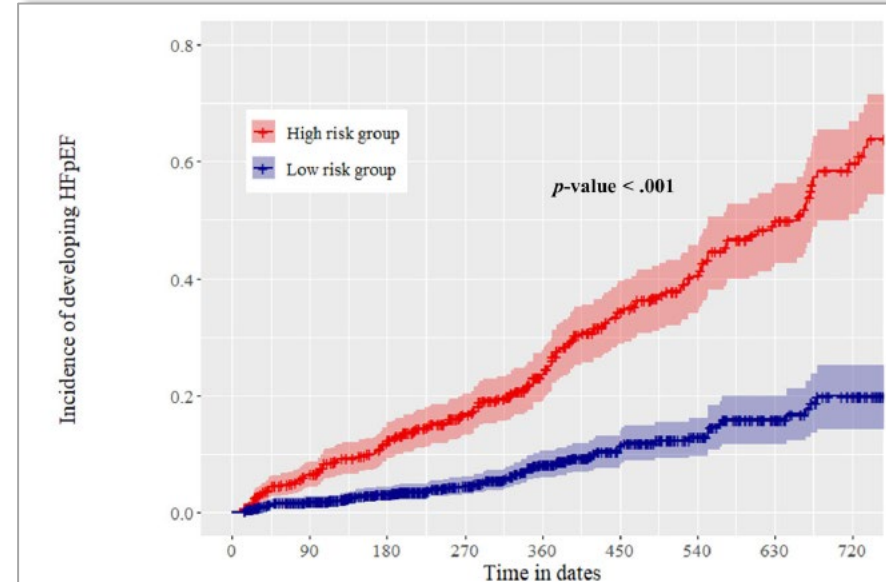
Sample 1: 32 671 ECGs of 20 169 patients (4048 with HFpEF) in Hospital 1
 Sample 2: 11 955 ECGs of 11 955 patients (1708 with HFpEF) in Hospital 2

AI ECG Diastolic Dysfunction Predicts Survival – Even When Echocardiographic Grade is the Same

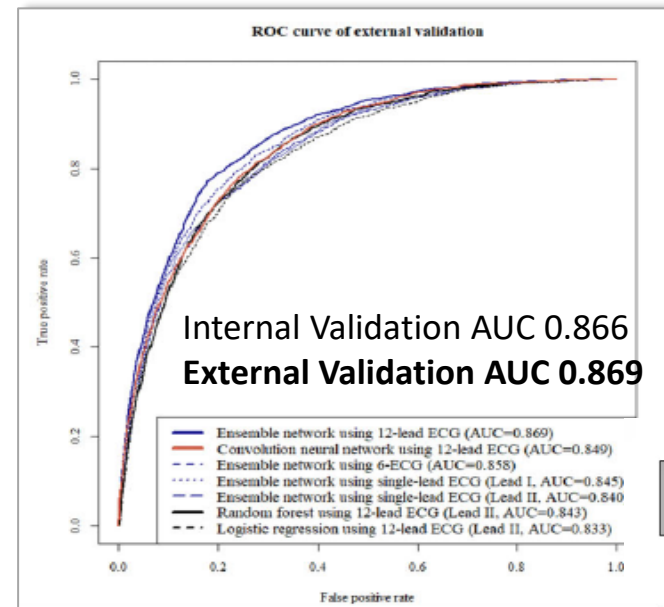
Eunjun Lee et al ACC 2023*



HFpEF development prediction



HFpEF detection among pts with normal LVSF



External validated DLM:
 PPV 42% NPV 96%

Atrial Fibrillation



Can AI Identify if SILENT AF IS PRESENT?

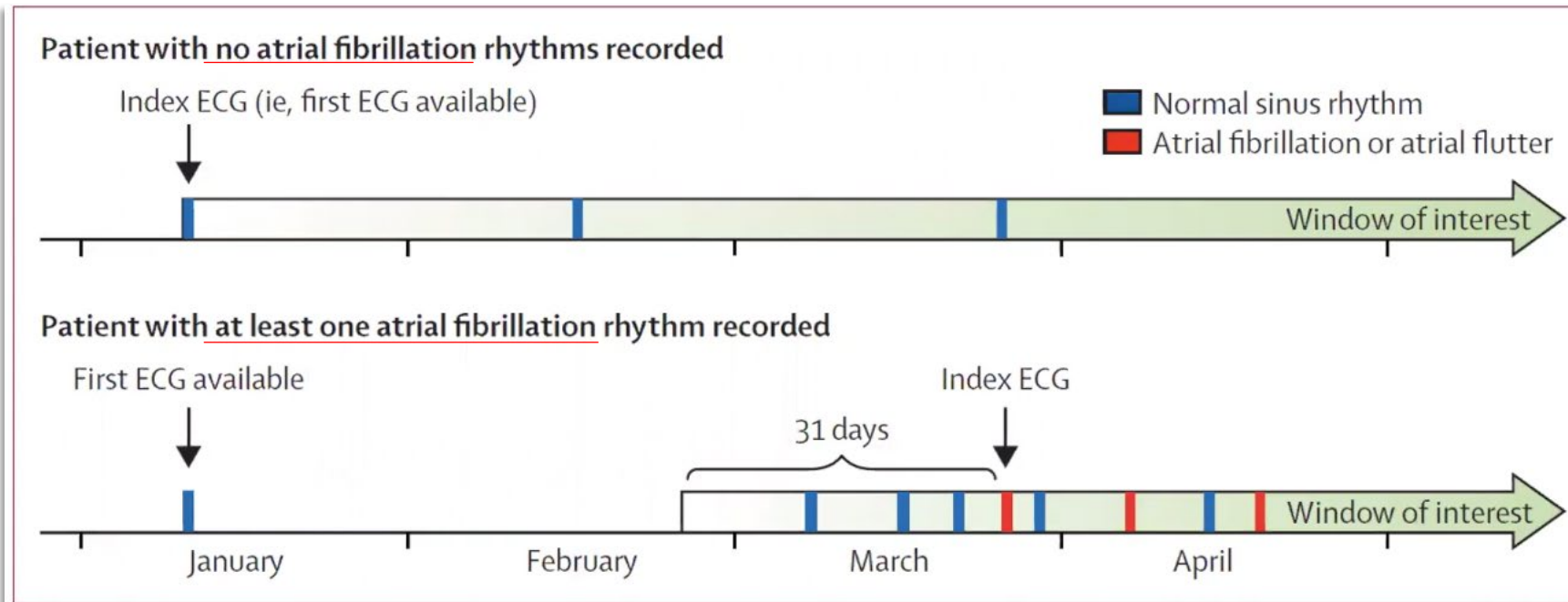
An artificial intelligence-enabled ECG algorithm for the identification of patients with atrial fibrillation during sinus rhythm: a retrospective analysis of outcome prediction



Zachi I Attia*, Peter A Noseworthy*, Francisco Lopez-Jimenez, Samuel J Asirvatham, Abhishek J Deshmukh, Bernard J Gersh, Rickey E Carter, Xiaoxi Yao, Alejandro A Rabinstein, Brad J Erickson, Suraj Kapa, Paul A Friedman

ATRIAL FIBRILLATION RISK CNN → to assess presence of silent AF during NSR

NETWORK only given NSR EKG, from 2 POPULATIONS: **AF and No AF**

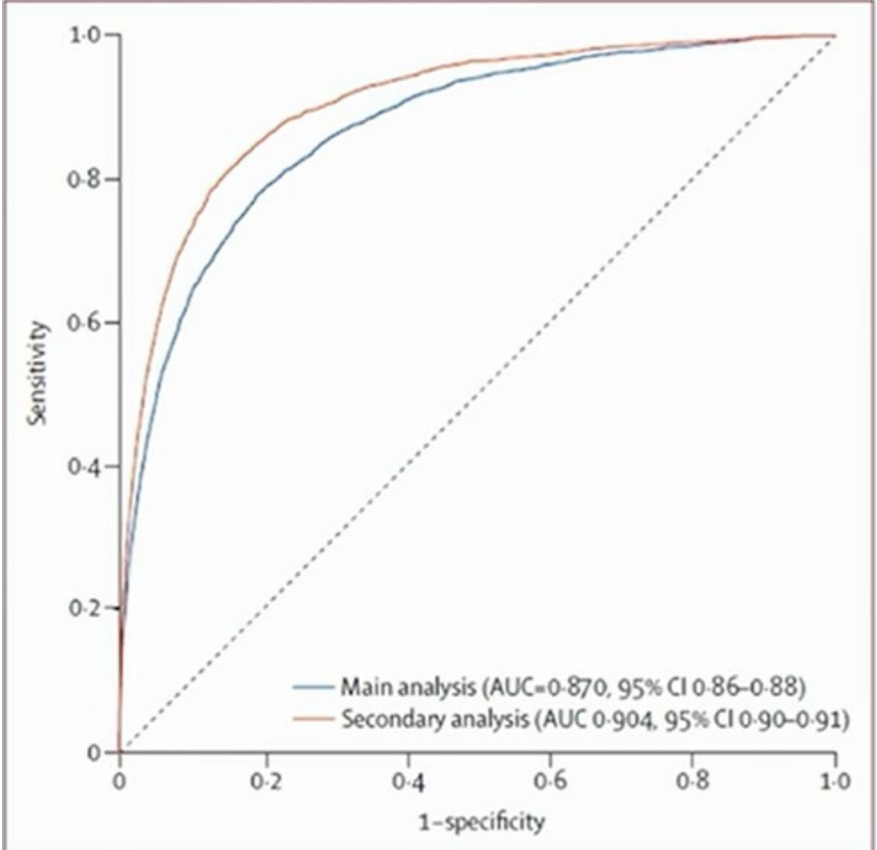


- **AI-EKG acquired during NSR permits identification of individuals with AF**
- **AI-EKG is strongly predictive of concurrent AF within 30 days of EKG during SR**
- **High degree of accuracy**



ATRIAL FIBRILLATION RISK: from an EKG recorded during Normal Sinus Rhythm → 'AF IS PRESENT ANOTHER TIMES'

AF risk from a Sinus rh EKG



AREA UNDER THE CURVE OF AF

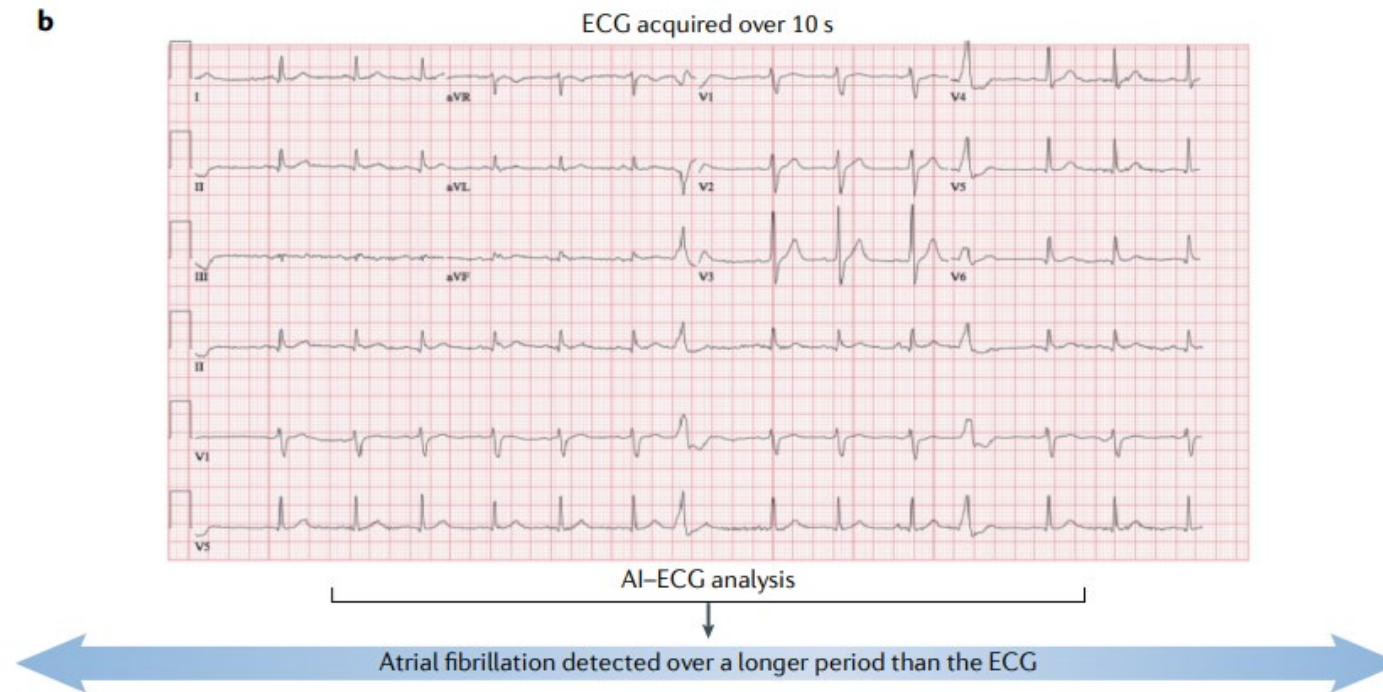
AUC – 0.90
PERFECT – 1.0

- AI-EKG is strongly predictive of concurrent AF within 30 days of EKG during SR



AI EKG – SINUS RHYTHM but AF IS PRESENT ANOTHER TIMES

AI converts a 10sec EKG into an ‘extended’ monitor to screen for SILENT AF



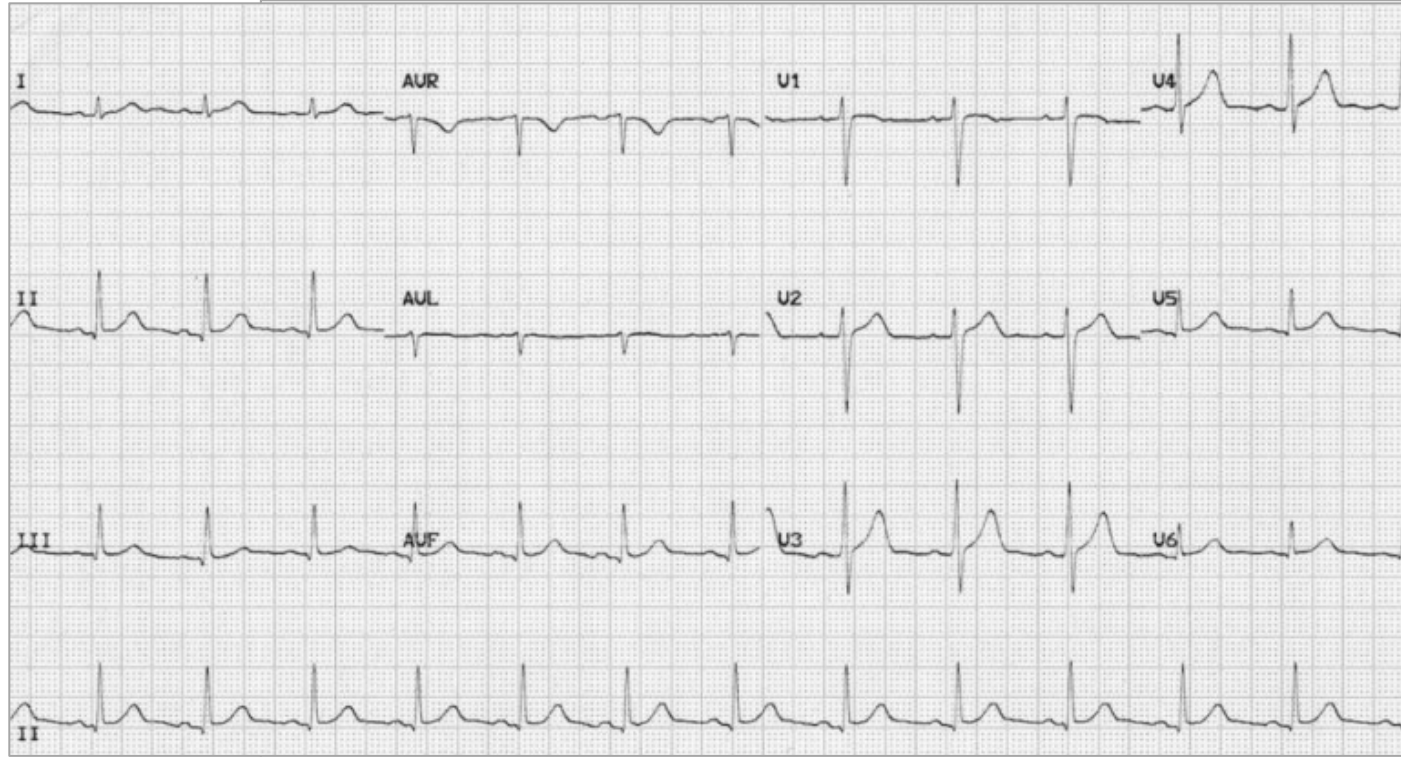
Screening
Diagnosing
Monitoring

SILENT AF DETECTION in SR

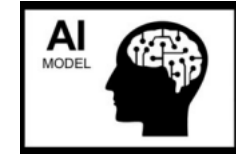
Stored EKG can be used as a “Holter” monitor

The AI-EKG AF probability progressively increases with time prior to the first AF episode

Case - 68Y M Retired MD, Hx T2DM, CKD



AI reading



Probability of AF 90%



Holter:
AF dx within 1 week



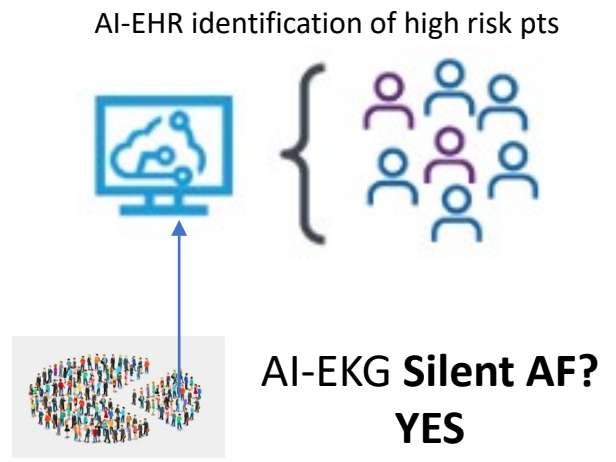
OAC

Future: Stroke
prevention?

→ Prospective trial designed to **detect silent AF** – high risk pts are in focus

AI-guided screening was associated with increased detection of atrial fibrillation (high-risk group)

Case - 68Y M Retired MD, Hx T2DM, CKD



- Prospective trial designed to **detect silent AF – high risk pts are in focus**
- **AI-guided targeted screening** approach (AI-EKG AF in SR? Y+ → NLP OAC? Y+ → 30d monitor)

Beagle study Batch Enrollment of and AI-Guided Intervention to Lower Neurologic event with Undiagnosed AF **CLINICAL UTILITY**

Retrospective - AI-EKG for Silent AF + Massive digital chart review
Prospective Remote digital monitor enrollment to confirm AF

Arrhythmia & Electrophysiology Review 2023;12:e12
[https://doi.org/10.1016/S0140-6736\(22\)01637-3](https://doi.org/10.1016/S0140-6736(22)01637-3)
Lancet 2022; 400: 1206–12; escardio.org

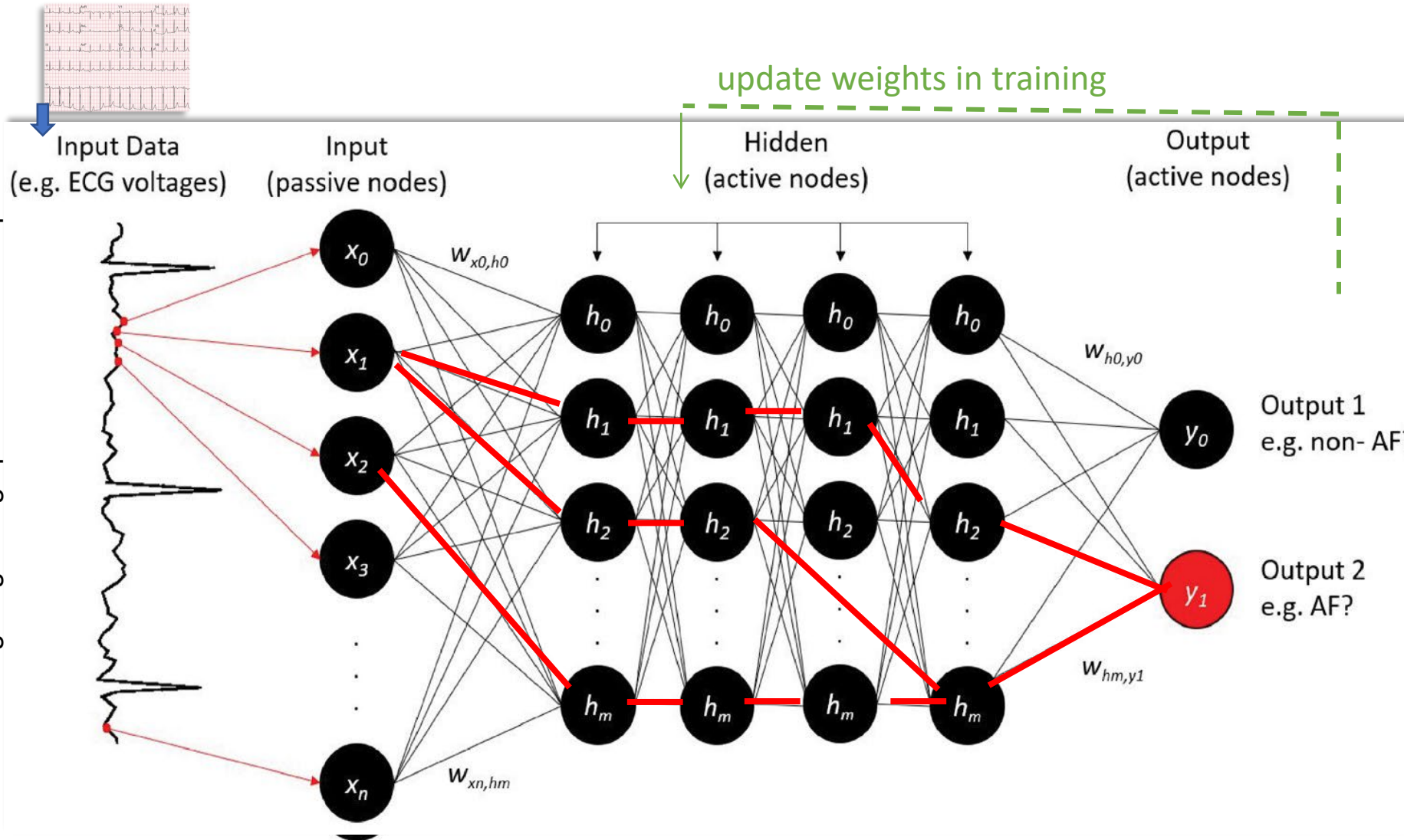
...insight to CNN training
METHODOLOGY

Neural network design to classify 'AF' from the EKG

Supervised learning (i.e.CNN)
Training to diagnose a known endpoint

- Match input to known output labels (dx, rx)

Continuous analog ekg voltage points are fed to 'input neurons



y0; incorrect, no AF

y1; correct AF

Neural network design to classify AF from the EKG

Repeat
100.000x

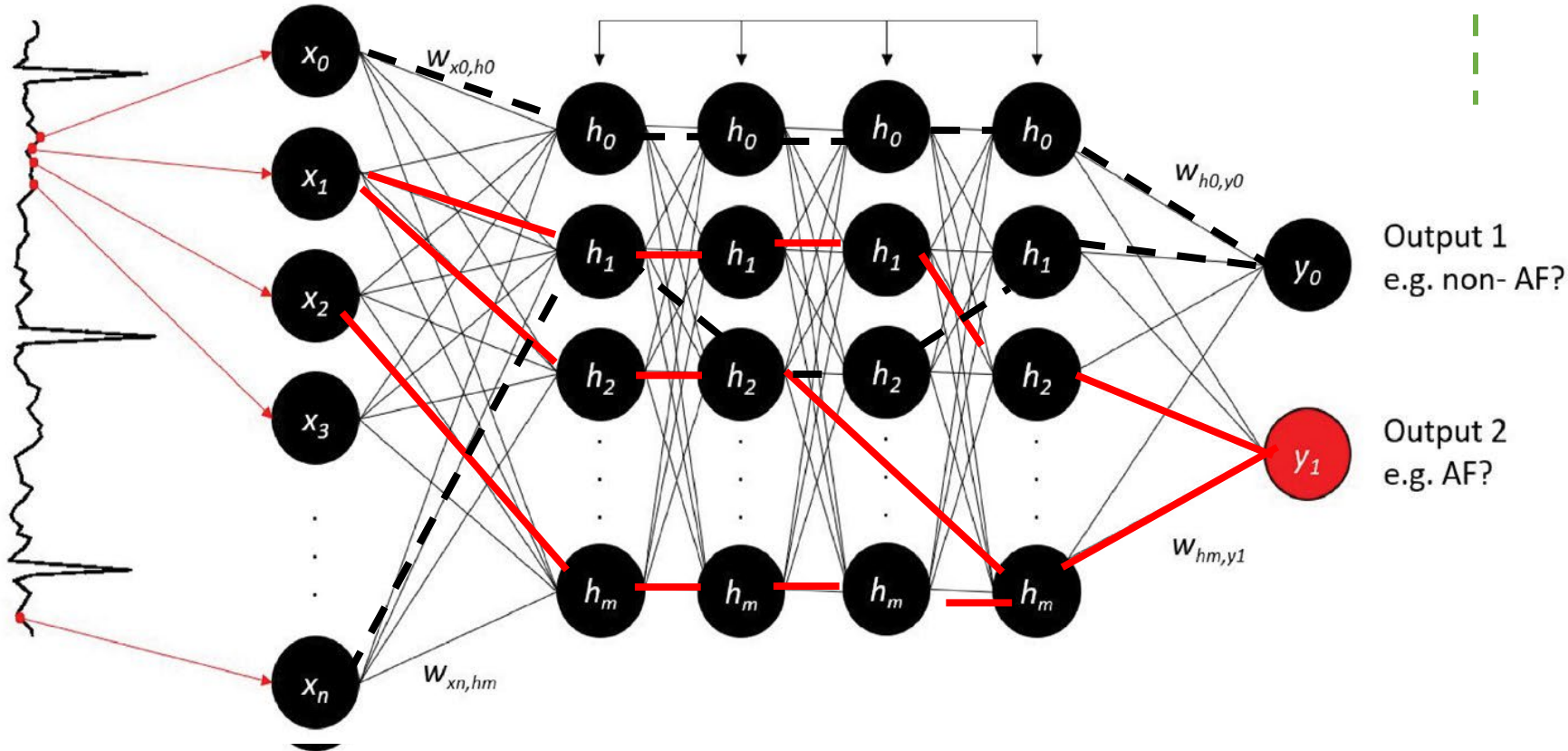
Input Data
e.g. ECG voltages

Input
(passive nodes)

update weights in training

Hidden
(active nodes)

Output
(active nodes)



Output 1
e.g. non- AF?

y0; incorrect, no AF

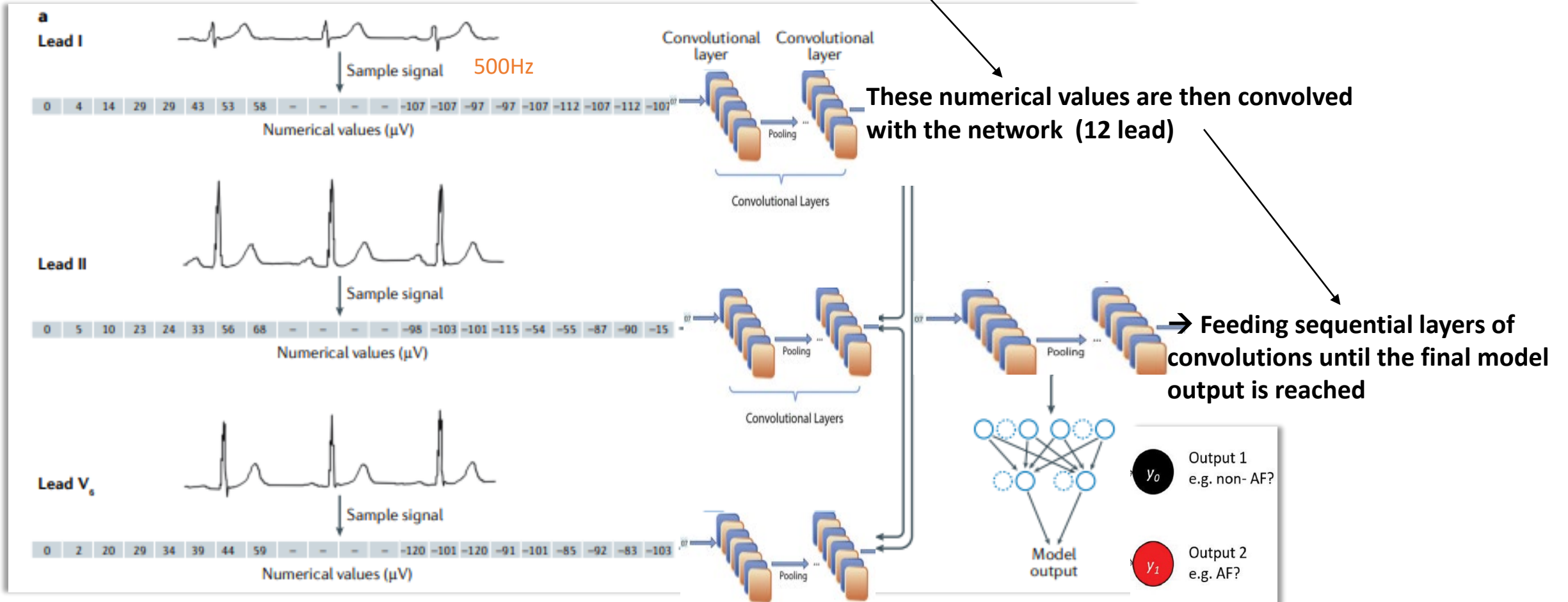
Output 2
e.g. AF?

y1; correct AF

Continuous ekg voltage points are fed to 'input neurons

Development of a CNN using the 12-EKG and application to detect silent AF

The analogue EKG signal is converted to a digital recording → numerical values corresponding to the amplitude of the signal



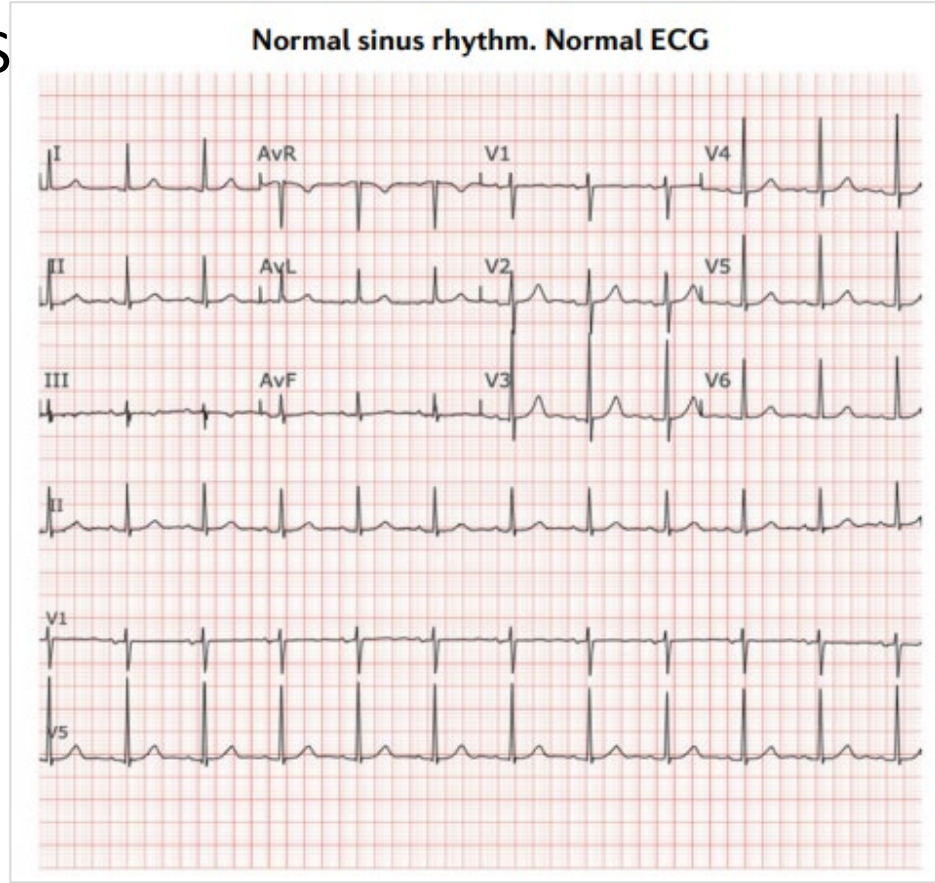
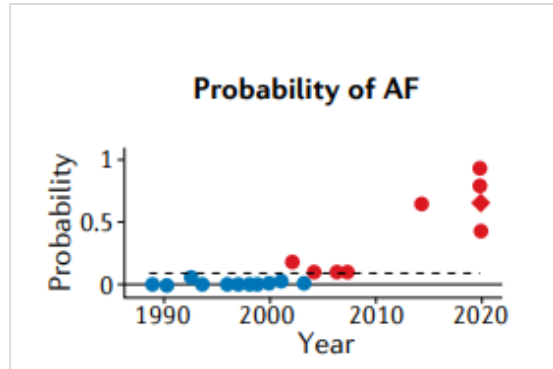
...CASES

...Cases

Positive - to predict Silent AF detection

Hx embolic stroke - undetermined source- ESUS

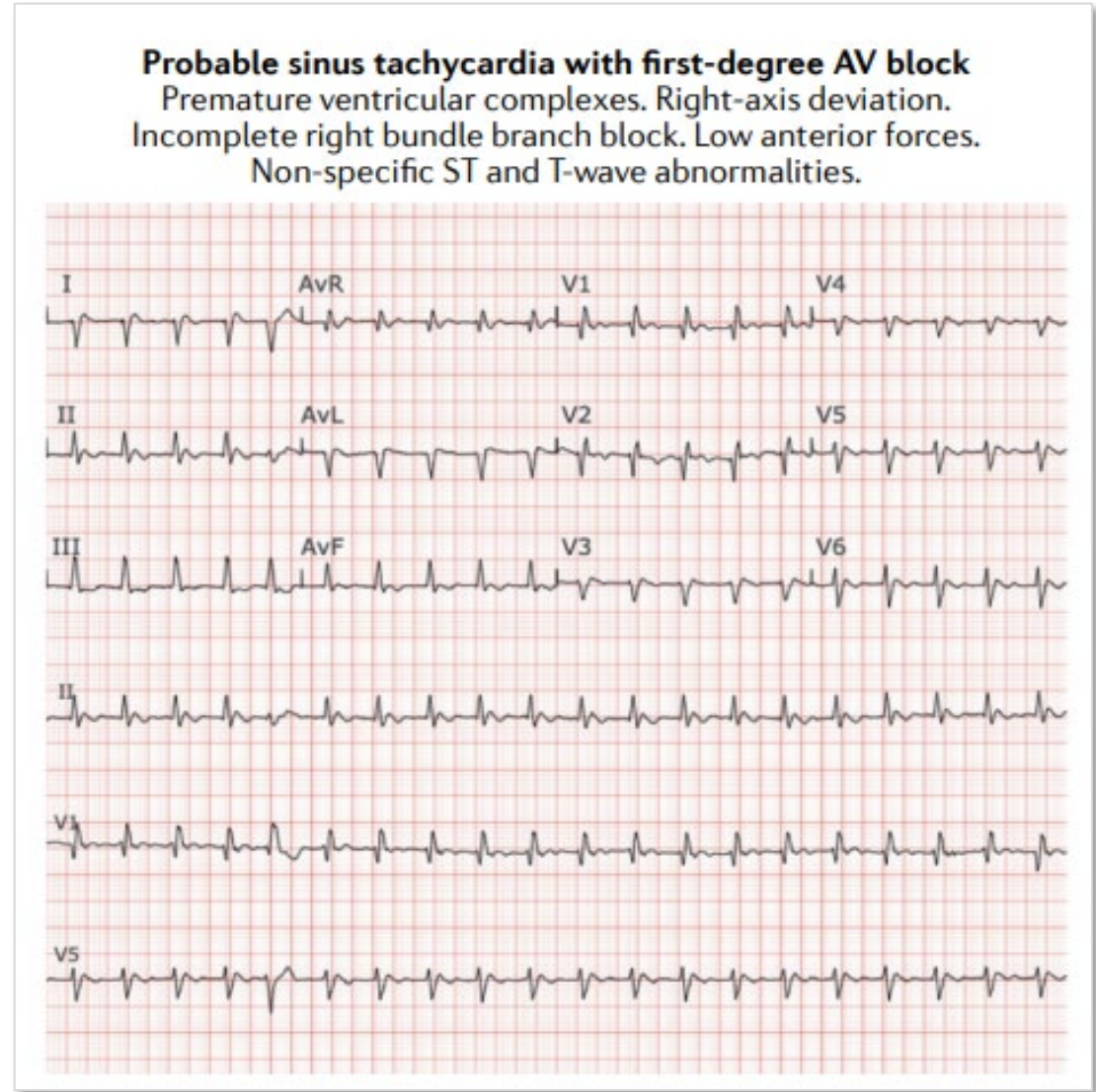
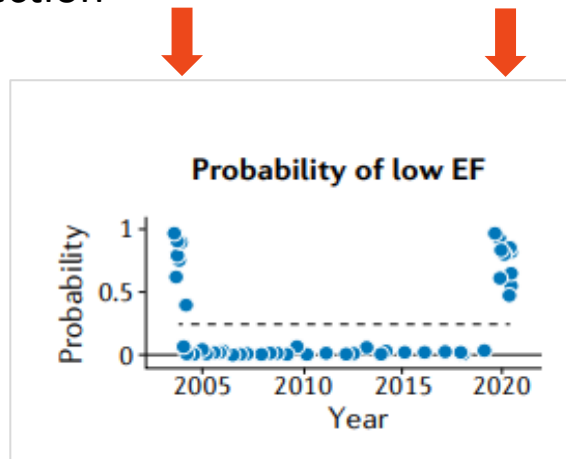
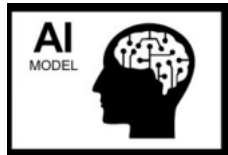
- increased probability of silent atrial fibrillation (red dots)
- predated the clinical documentation AF



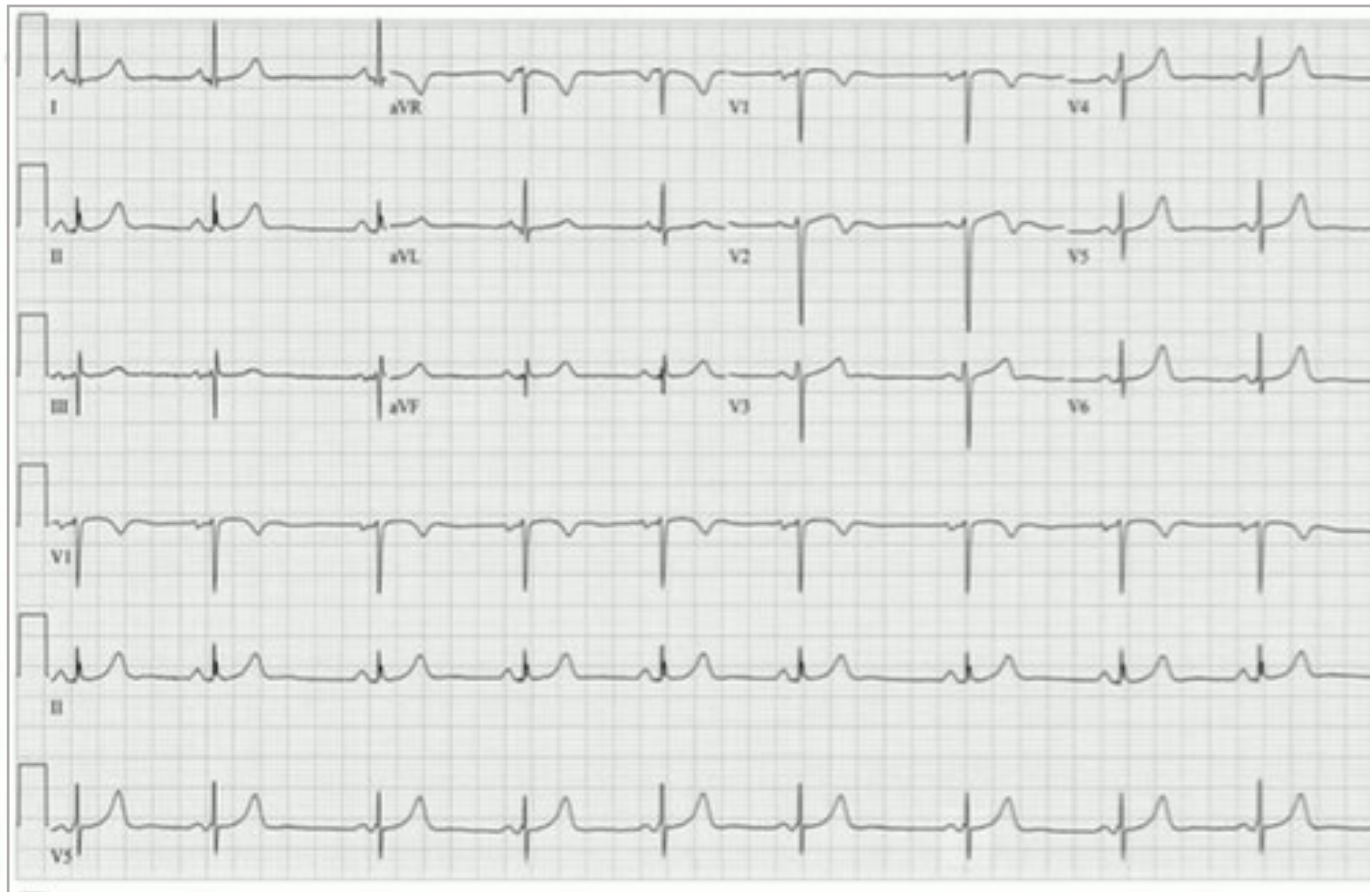
...Cases

Hx of heart transplantation in 2005 and graft rejection with LVSD in 2020.

AI-EKG reported a high probability of low ejection fraction (EF) x2 correlating with the graft rejection

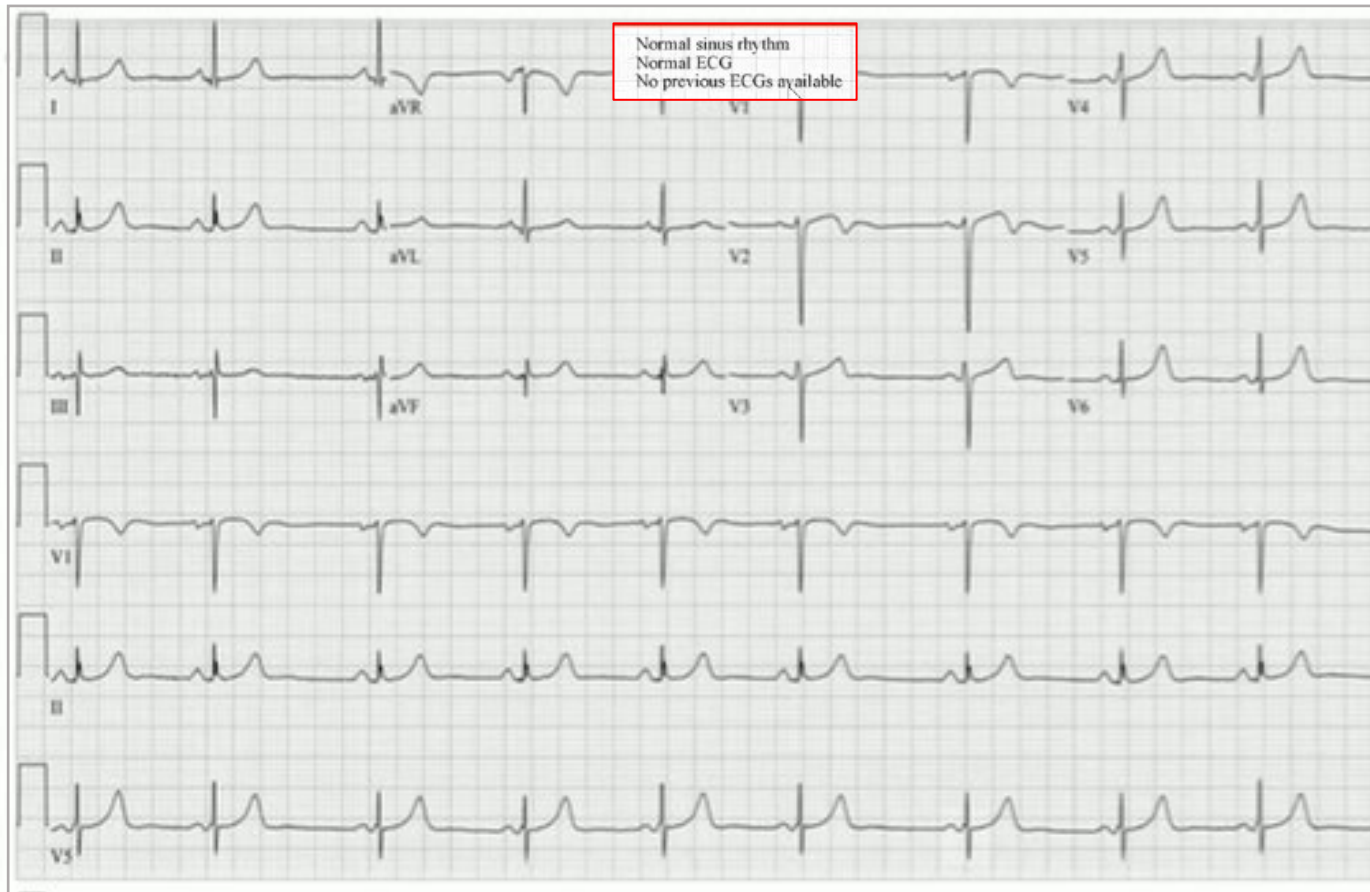


26y F No history / No history provided



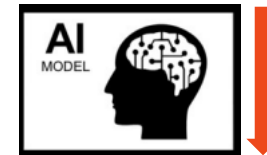
What do you think about this EKG?

26y F



- Computer reading: Normal
- Human reading:
~ minor abnormality

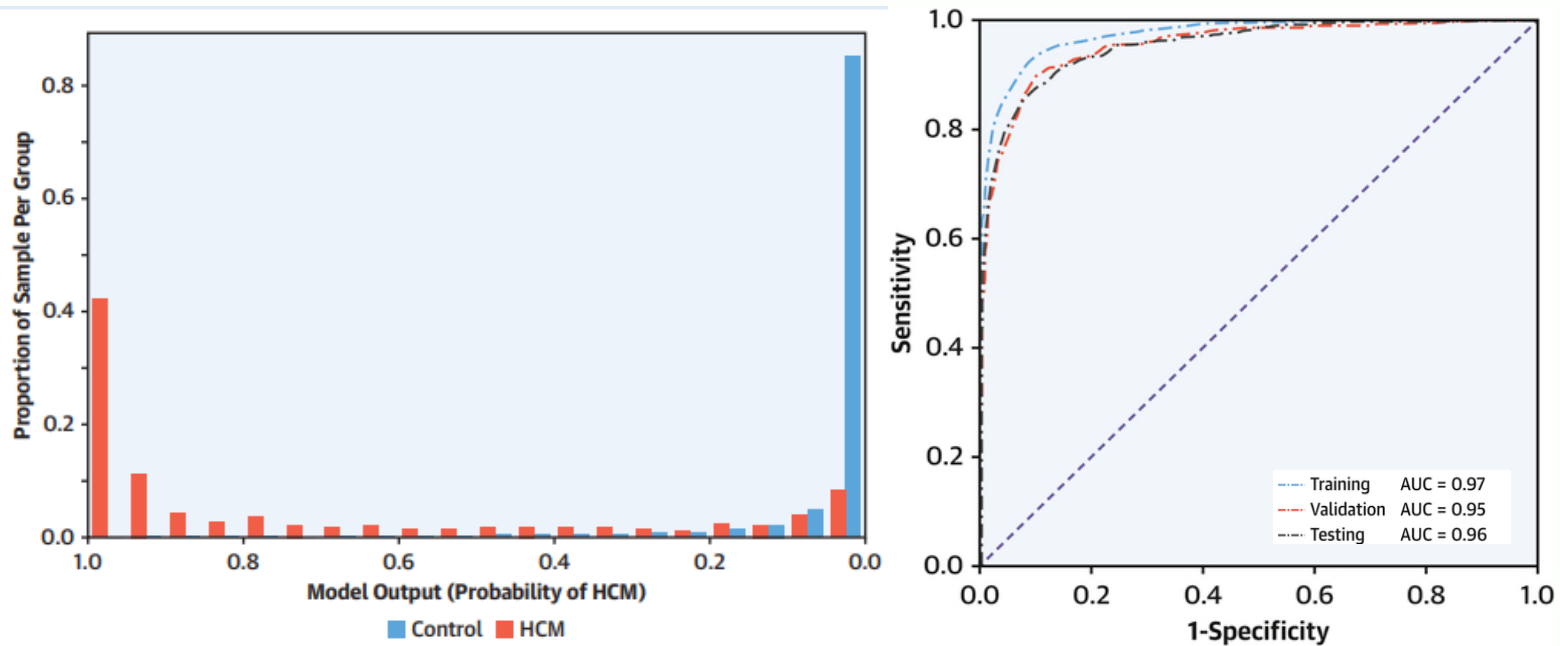
AI reading



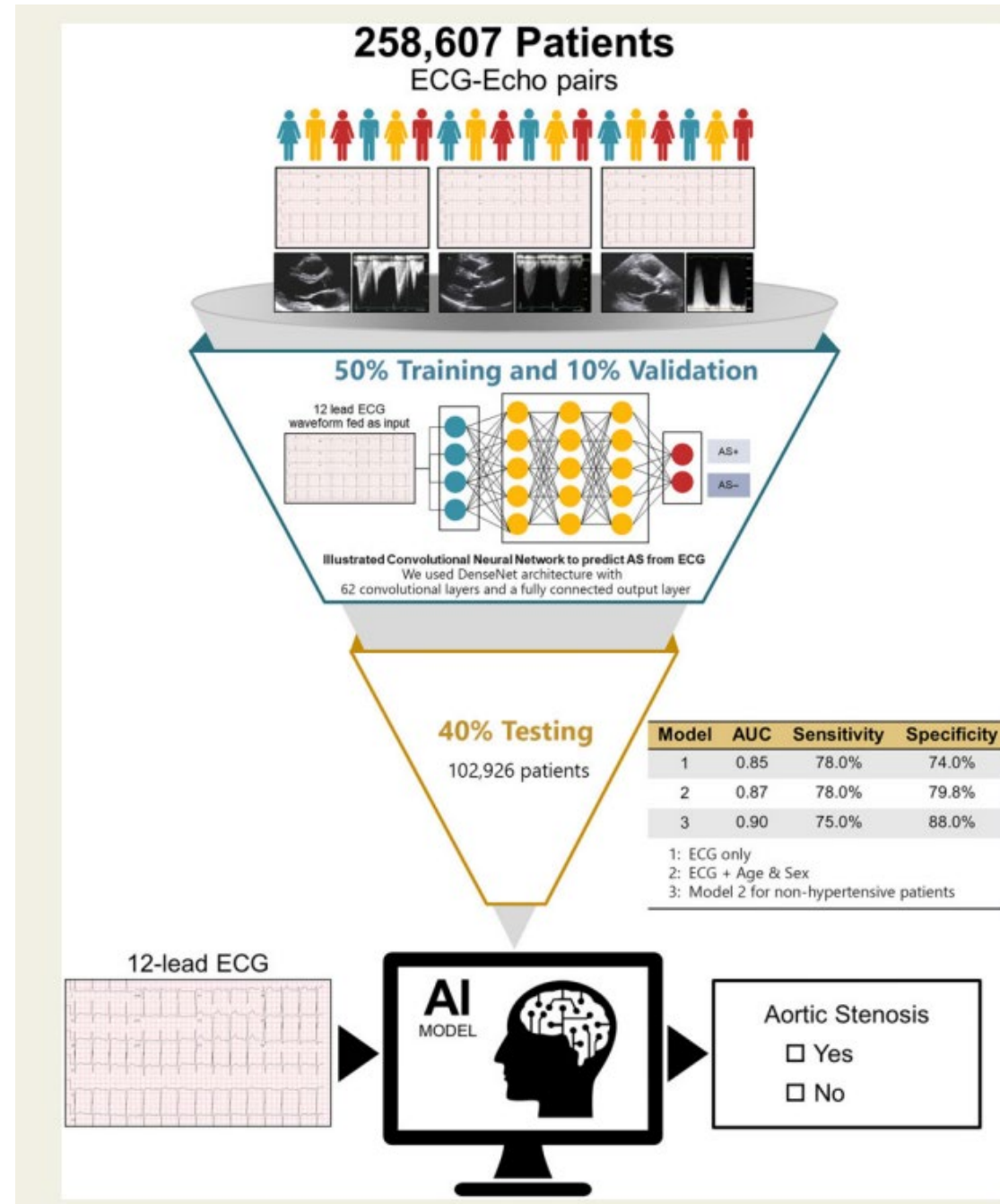
Probability of HCM 72.6%

Echo: HCM

HCM: MODEL PERFORMANCE

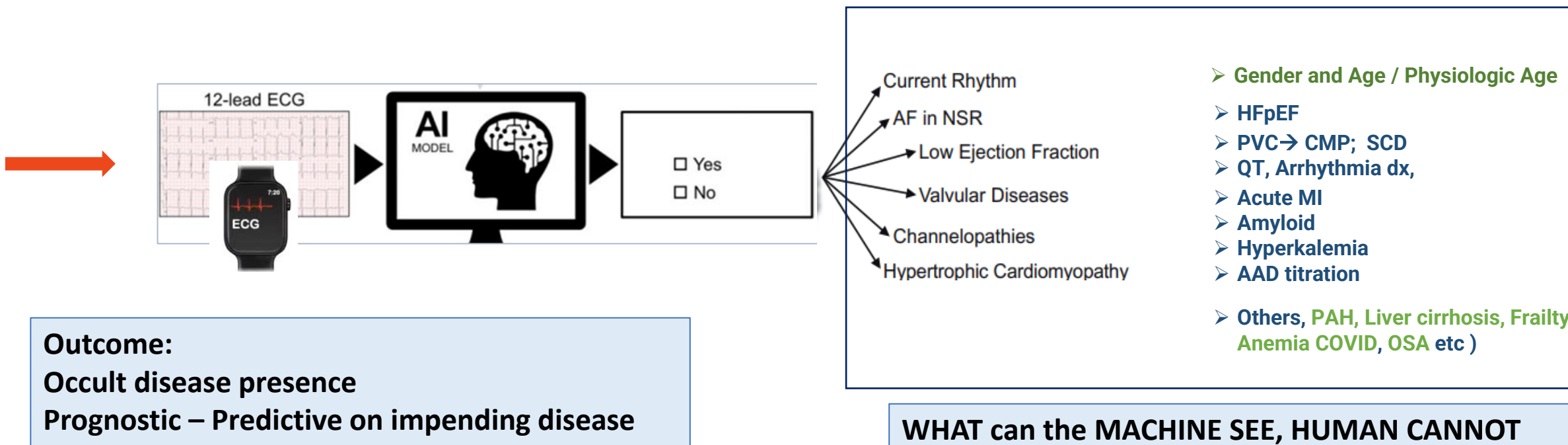
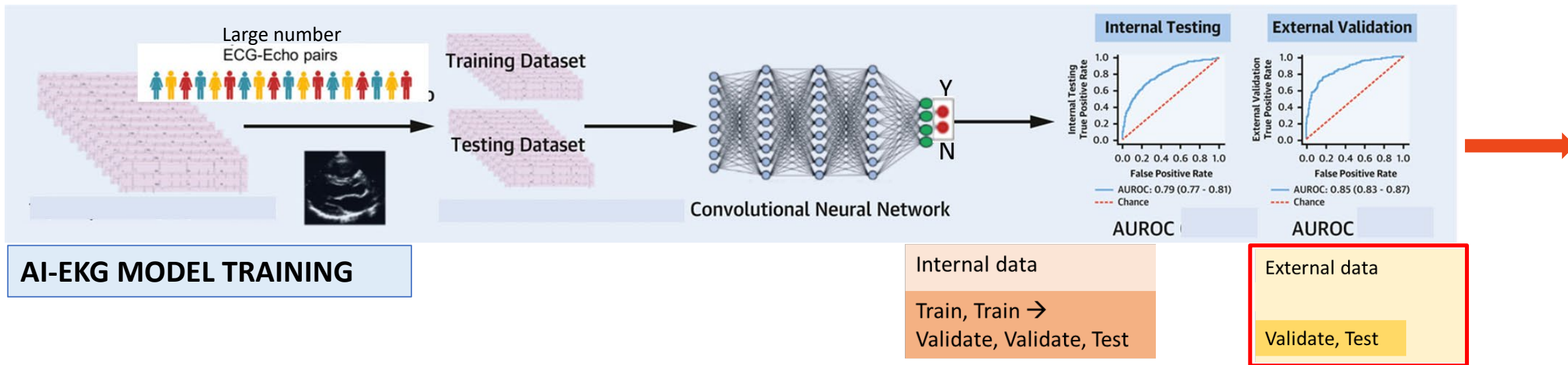


AORTIC STENOSIS



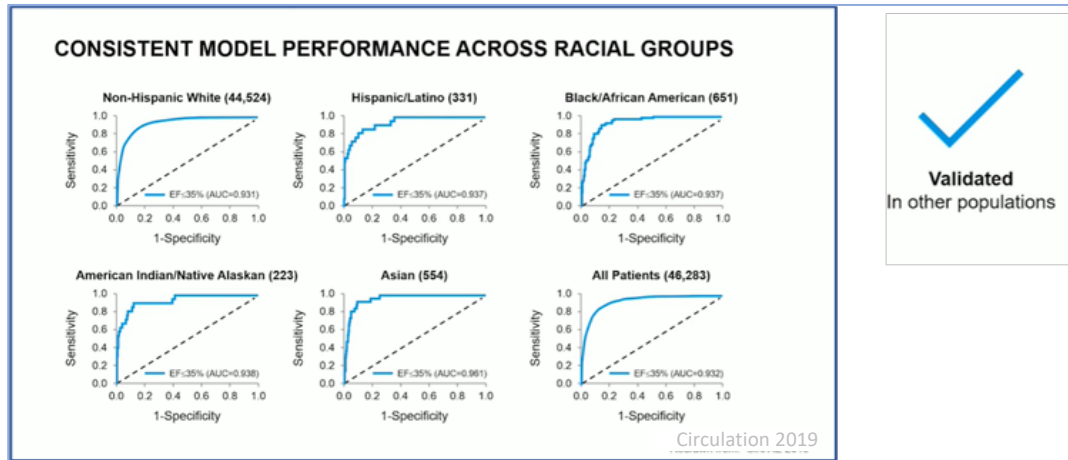
OVERVIEW

AI-EKG OVERVIEW

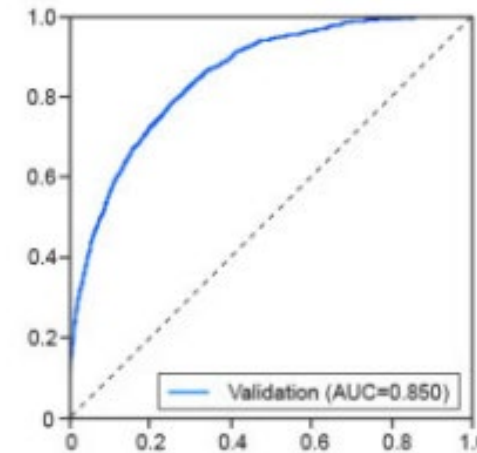


AI-EKG OVERVIEW -- PERFORMANCE

DETECTION OF LOW EJECTION FRACTION- 12 LEAD

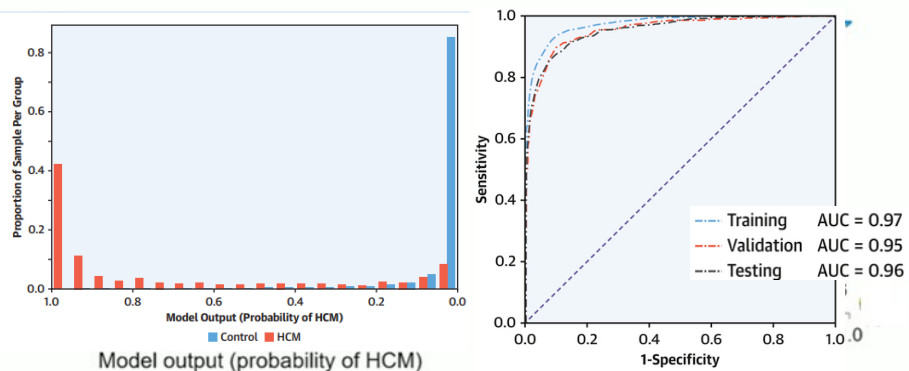


AORTIC STENOSIS PERFORMANCE



Eur Heart J. 2021 Aug 7;42(30):2885-2896. doi: 10.1093/eurheartj/ehab153.

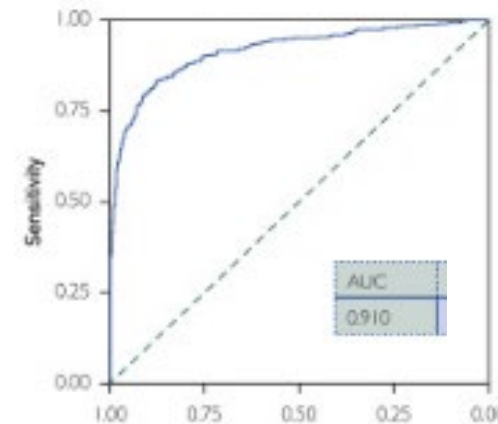
HCM: MODEL PERFORMANCE



HCM- Int J Cardiol. 2021 Oct 1;340:42-47. doi: 10.1016/j.ijcard.2021.08.026

Amyloidosis PERFORMANCE

Model Performance



Mayo Clin Proc. 2021 Nov;96(11):2768-2778. doi: 10.1016/j.mayocp.2021.04.023

MULTIPLE RELEVANCE - RICH PIPELINE OF AI TOOLS

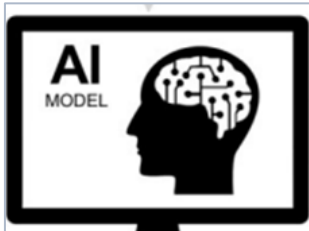
CONSISTENT FINDINGS

AI-EKG find Occult disease

AI EKF Predicts disease before clinically detected

Prediction - recurrent pattern

- LVD
- AF
- AS
- Amyloid
- Liver cirrhosis



NEW EFFECTIVE DRUG TREATMENT AVAILABLE

- LVD
- HYPERTROPHIC CMP
- AMYLOID HEART DISEASE
- PULMONARY HTN

UNDERDIAGNOSED – MORBIDITY IMPLICATION

- LVD
- HYPERTROPHIC CMP
- EPISODIC AF
- OTHERS..

SCREENING DISEASES

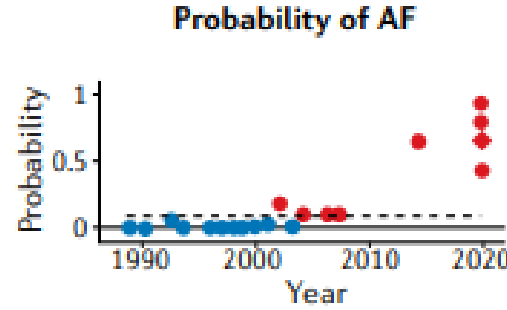
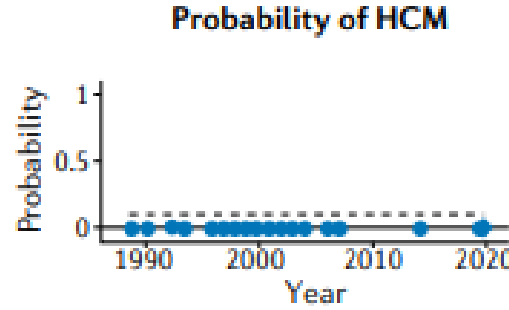
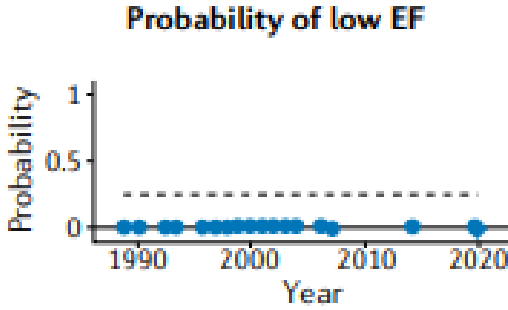
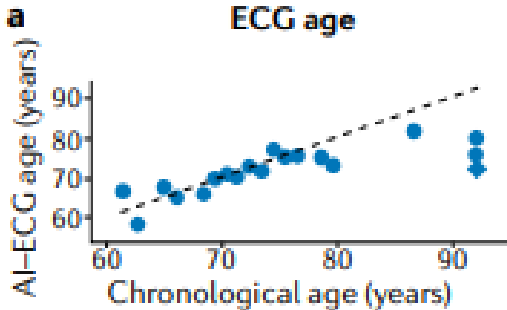
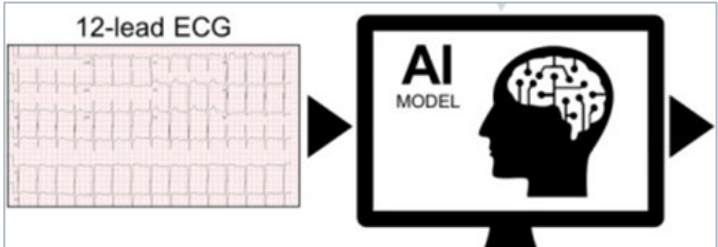
PREVALENT DISEASES

- LVD (AUC 0.93)
- AS (AUC 0.85)

RARE DISEASES

- HCM (AUC 0.96)
- AMYLOID HEART (0.91)
- Peripart CMP (0.87-.92)

MULTIPLE SIMULTANEOUS ALGORITHMS



MULTIPLE WAYS TO GET SIGNALS

Kardia

Record EKG
25 mm/s 10 mm/mV

84 BPM

18

Great Signal

Record EKG
Great Signal 24 70 BPM

Electrocardiogram (ECG)

AvR V1 V4
AvL V2 V5
AvF V3 V6

76 BPM 10:09

24sec

It helps to rest your arms on a table or your legs.

AI
Screens for EF

15 seconds

Study in progress

- ✓ No Murmur Detected
- ✓ Normal Sinus ECG Rhythm
- ✓ Normal EMAT
- ✓ Normal Ejection Fraction

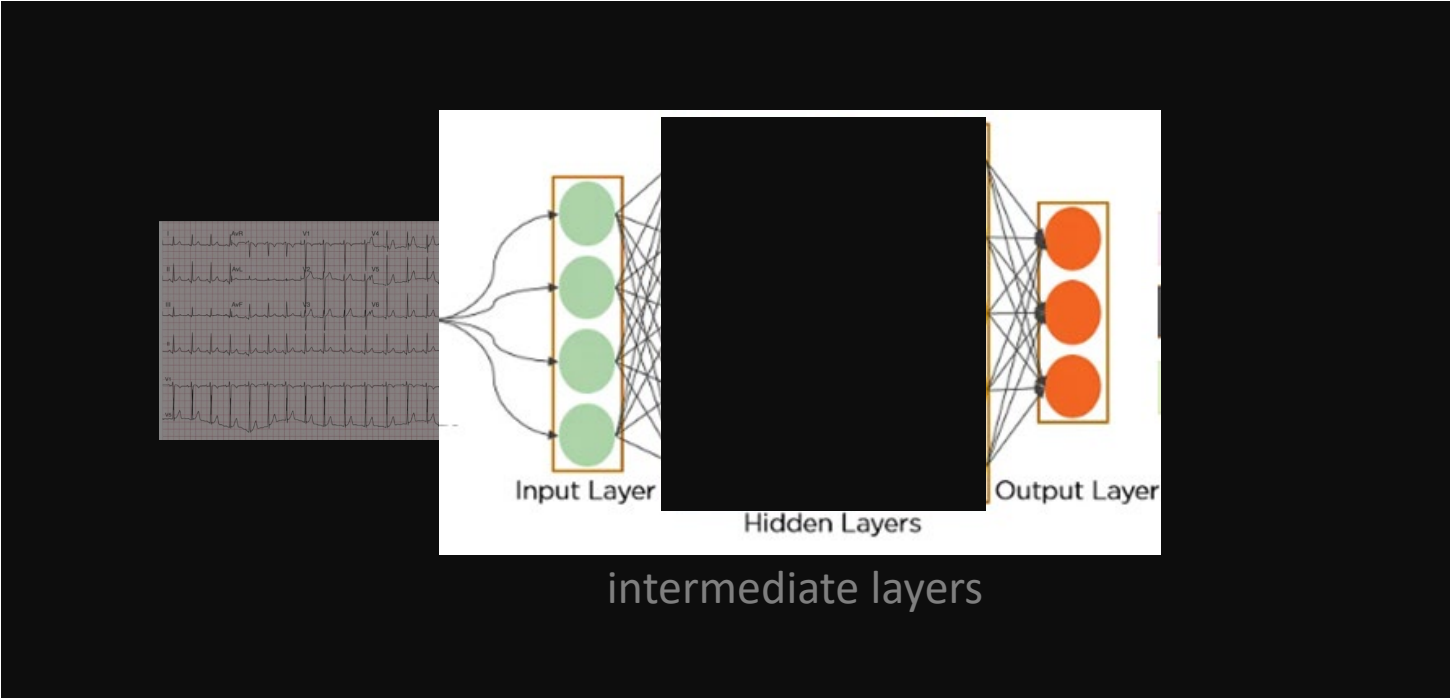
Anal of E

MULTIPLE CHALLENGES

- Barriers of AI-EKG (Barriers to AI-EKG Adoption: Algorithm generalizability, implementation, utility)
- Data label accuracy: robustness of data labels used for training and testing
- Risk of bias: cohort creation and controls, formulating q , poor input data
- Overfitting/lack of generalizability
- Data privacy, (sharing) Regulations, Replicability, Standardization
- Transparency. Trust and *many more..*
- **Explainability**

What does the Machine see in the EKG?

Lack of transparency



BLACK BOX

humans cannot understand how the network makes its decisions

EXPLAINABILITY

uncovering the underlying rules

What does the Machine see in the EKG?

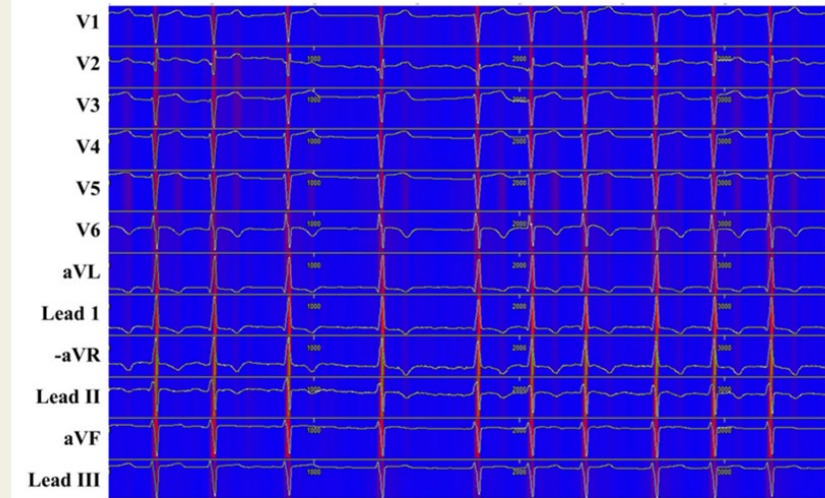
→ Other techniques

→ SALIENCY MAPS

highlight the portions of the EKG that contributed to the model's output in selected samples.

LVD pEF

European Heart Journal - Digital Health (2020) 2, 106–116



Sensitivity map of deep learning model for detecting HFpEF. HFpEF, heart failure with preserved ejection fraction.

AS

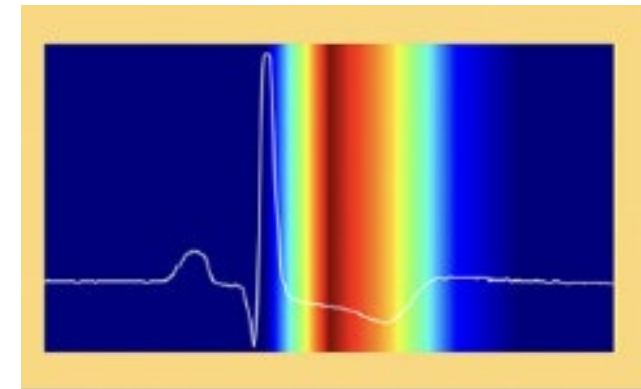
European Heart Journal (2020) 42, 2885–2896
doi:10.1093/eurheartj/ehab153

Electrocardiogram screening for aortic valve stenosis using AI



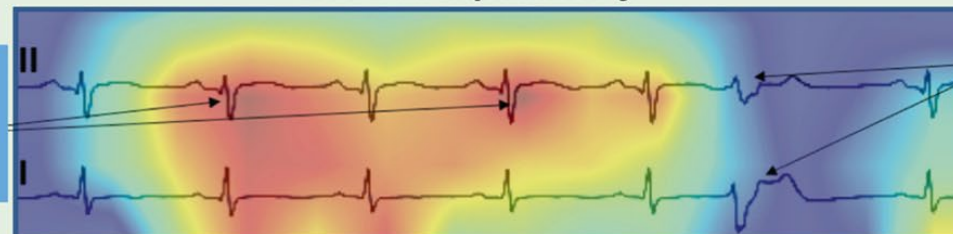
Saliency map. A representative electrocardiogram example for true positive is shown. Probability of moderate or severe aortic stenosis by artificial intelligence electrocardiogram is 0.92 in the presented case. The blue lines are the 'saliency' guiding the selection of attended locations.

HCM - Single lead



GradCAM Explainability

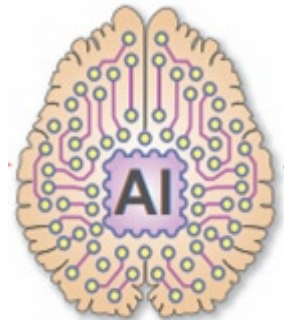
GradCAM highlights the sinus rhythm QRS complex and ST segment in red.



The PVC morphology is not highlighted as an important feature for model prediction.

PVCs

AI-EKG – SUMMARY



AI has the potential to completely change the way physicians use EKG

POTENTIALLY: Powerful, non-invasive Biomarker -- Digital assistant tool

- Identify occult diseases
- Predict impending diseases
- Screening
- Monitoring
- Deep phenotyping
- Identify At-Risk Phenotypes
- Age and sex determination
- AI-EKG guided management
 - TBDetermined: direct rx based on EKG
 - tailor triage, work flow, investigations,
 - more precise and earlier treatment,
 - Personalized treatment selection, monitoring

CLINICAL
UTILITY



PREDICT
DETECT



MASSIVELY
SCALABLE



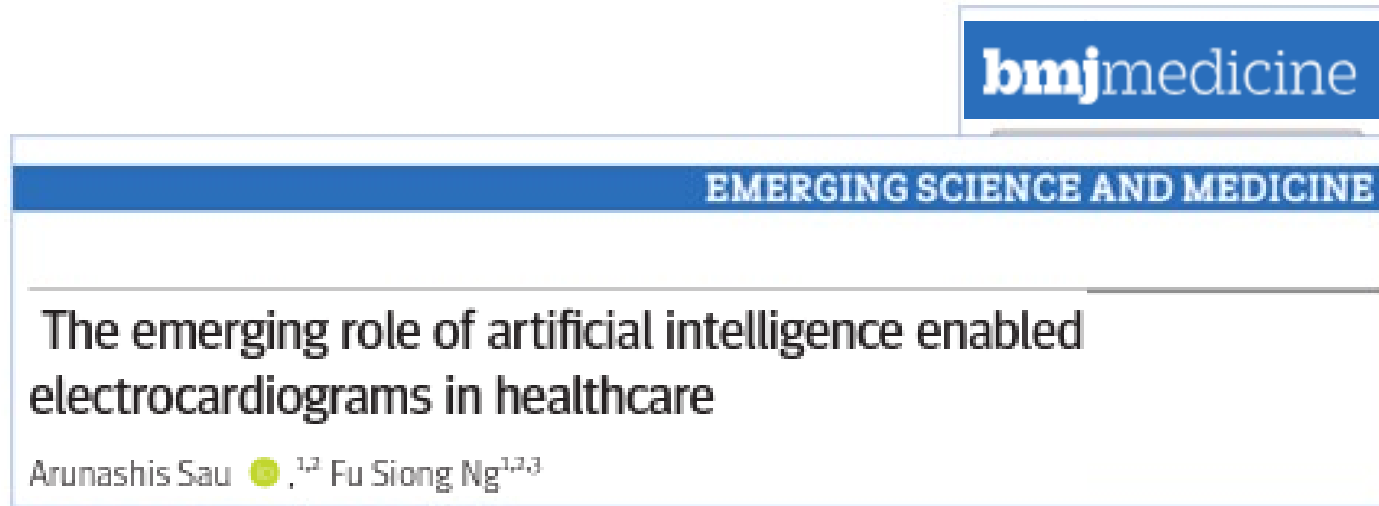
TRANSATE TO PRACTICE
DRIVES INNOVATIONS



- Is **massively scalable**
 - Require testing, vetting and validation
 - Can improve resource utilization
 - Deployable across many form factors
- Further innovations // Translate to Practice**

Can be run from a smart phone - Widely available, **inexpensive**, test, **Massively scalable**

AI-EKG - The Present Situation - 2023

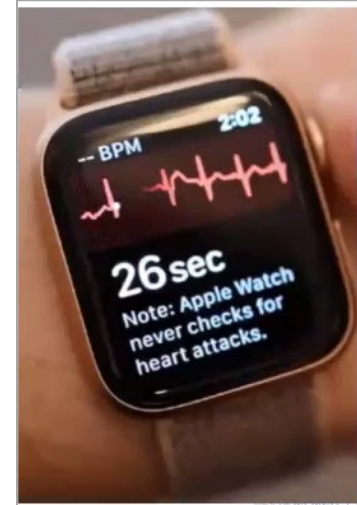


- AI enabled EKG is **Not** currently ready for clinical use
- AI has the potential to completely change the way physicians use electrocardiograms
- It **could transform clinical care** of patients with cardiovascular disease, promoting early detection, prediction and tailored therapy
- **Advancements should be made with caution because of several potential pitfalls** with the rapid growth of artificial intelligence enabled electrocardiogram applications
- Great care must be taken to ensure the **implementation** of AI enabled EKG is done **safely and ethically**

The Present Situation of AI-EKG?

BE SMART

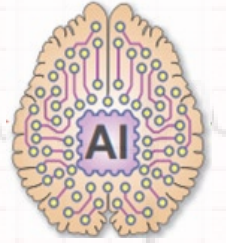
WATCH and WAIT



Advancements should be made with caution -- potential pitfalls with the rapid growth of AI enabled EKG applications

→ Multiple center collaboration is being deployed..

QUESTIONS



THANK YOU!