

# Digital health innovation in cardiology



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## Introduction

At its core, cardiology is a data-driven specialty with routine practice relying heavily on insights from both clinical trials and individual patient-level data. Rapid innovation in cardiac digital health is inevitable when one considers the vast amounts of standardized, high-quality digital data collected during routine clinical practice and, increasingly, from consumer-facing sensors in nonclinical settings. These vast amounts of data present the field with several opportunities and challenges. The additional information offers the potential to improve remote monitoring, provide point-of-care diagnoses, guide treatment, and facilitate screening efforts. Conversely, the volume can overwhelm cardiology teams. Machine learning (ML) and extended reality (ER) are being embraced to bridge these 2 divergent positions. In this perspective, we explore the growing role of these 2 technologies in cardiology with an emphasis on electrophysiology (EP). We also provide a window into cardiovascular innovation at Mayo Clinic, including its response to the COVID-19 pandemic.

## Artificial intelligence in cardiology

Broadly speaking, artificial intelligence (AI) refers to the ability of machines to autonomously learn, reason, and act using a variety of tools. It is a nontechnical term that typically refers to ML—computer algorithms that are able to independently find patterns in large amounts of data.<sup>1</sup> Deep learning, a subfield of ML, uses neural networks to find these patterns and learn the relationships between provided input and desired outcomes. ML is already being employed in all cardiology subspecialties, with applications ranging from workflow optimization to disease diagnosis

and prognostication, therapeutic intervention decision support, and research.<sup>1</sup> Its uptake has been directed at 2 general goals: (1) providing human-like capabilities at scale and (2) developing new insights by analyzing existing data sets individually or in novel combinations (essentially moving beyond current human capacity).

ML application to output of clinical-grade ambulatory monitors (eg, implantable loop recorders, Holter monitors, pacemakers/defibrillators, etc) and commercial heart rate monitoring devices can scale the cardiologist's reach by analyzing data from prolonged monitoring and flagging only critical results for human review. When combined with natural language processing, it can also optimize workflows by generating reports (eg, electrocardiogram [ECG] interpretation) that are indistinguishable from the cardiologist's. In the EP laboratory, ML is being deployed to remove noise from intracardiac tracings, thereby simplifying their interpretation.

The application of ML to ECGs provides one of the most compelling examples of generating novel insights from existing data. It can estimate serum potassium and dofetilide levels, identify patients with atrial fibrillation by analyzing sinus rhythm ECGs, predict patients' left ventricular ejection fraction, detect hypertrophic cardiomyopathy, and identify patients' sex and age.<sup>2–9</sup> The left ventricular ejection fraction algorithm has been modified to work using a single-lead ECG produced by devices such as the Eko Duo,<sup>10</sup> AliveCor Kardia, and Apple Watch (unpublished). Although these novel ECG insights are exciting, there is limited information on how they will perform in real-world settings. The ECG AI-Guided Screening for Low Ejection Fraction study (NCT04000087), a pragmatic 2-arm cluster randomized trial, should provide initial answers. It will evaluate the use of the aforementioned AI enabled, 12-lead ECG-based tool to screen for low ejection fraction across multiple primary care settings.<sup>11,12</sup> The Batch Enrollment for AI-Guided Intervention to Lower Neurologic Events in Unrecognized AF study (NCT04208971) will similarly test the performance of the AI-enabled, 12-lead ECG-based tool to improve the diagnosis of unrecognized atrial fibrillation and stroke prevention. Finally, screening for contractile dysfunction via 12-lead ECG using AI has recently received

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emergency use authorization from the FDA for deployment during the COVID-19 pandemic. In the future, it is possible that ML will be used to cost-effectively diagnose a range of other cardiovascular conditions from the ECG, thereby improving population health. Eventually, ML (eg, using synergistic networks) will be able to incorporate inputs from varied data sources (eg, ECGs, imaging, phonocardiograms, etc) into a single output.

### Extended reality

ER refers to the spectrum of immersive technologies ranging from fully immersive digital environments to projections of digital structures onto the physical environment. It currently includes virtual, merged, mixed, and augmented realities.<sup>13</sup> Its uptake within cardiology is being driven by rapid advances in computing and display technologies, which have improved their real-time responsiveness while simultaneously decreasing their costs and physical profiles.

ER can facilitate cardiology education, procedure planning, and execution by bringing mentally constructed 3D cardiac images closer to the physical realm. It has been deployed for procedural planning (eg, lead extraction) and execution (eg, cardiac ablation). Holograms of prior cardiac imaging, high-resolution scar architecture, real-time electroanatomic maps, catheter positions, local activation timing maps, and ablation lesion markers can be projected above the patient during EP procedures.<sup>13,14</sup> The proceduralist and other team members are able to interact with these 3D images in a touchless manner to facilitate the procedure.

### Mayo Clinic cardiovascular innovation Organizational structure

Like other large academic medical centers, Mayo Clinic has distinct structures to execute its clinical, research, and education missions. While innovation is critical to each of these, it may be lost among the many competing priorities within these structures. A unique organizational structure was therefore created to ensure that innovation is central to and coordinated across all activities within the Department of Cardiovascular Medicine. Key elements to this structure include the following:

- An administrative partner with deep understanding of business, financial, regulatory, and operational impacts of innovation is paired with the physician leading innovation to facilitate sound decision-making.
- Nonclinical team members are embedded within the clinical team. For example, AI engineers accompany physicians on daily activities and co-locate with them while device prototype development engineers participate in experiments. AI engineers are also hired using the same process as cardiologists.

### Mayo Clinic cardiovascular innovation and COVID-19

Our response has focused on using ML to prognosticate SARS-CoV-2 infections while developing a novel technology to facilitate rapid, consistent, and safe point-of-care decontamination of personal protective equipment (PPE). We have also developed ECG lab infrastructure leveraging AI-ECG to monitor the QT interval in patients undergoing experimental treatments within prospective clinical trials using the AliveCor Kardia platforms.

### Leveraging machine learning to diagnose COVID infections using ECGs

SARS-CoV-2 infection is known to involve the cardiovascular system, with accompanying nonspecific ECG changes seen very early during the infection. We are currently leading a global effort exploring the use of ML interrogation of ECGs to prognosticate COVID-19 infections. The ability to stratify COVID-19 infection severity could inform where patients may be safely treated and when they can be safely discharged. This could have profound implications on optimizing resource use by already stressed healthcare systems.

### Developing a point-of-care sterilization tool to facilitate PPE reuse

Pulsed electric fields (PEF) refer to the application of intermittent, high-intensity electric fields for short periods of time. Depending on several factors, this results in reversible or irreversible disruption of cellular membranes. PEF has been shown to inactivate both enveloped and nonenveloped viruses and our preliminary data suggest that viruses similar to SARS-CoV-2 are inactivated when exposed to PEF. This insight is being used to develop a PEF-based sterilization tool that may be combined with more established sterilization modalities (eg, ultraviolet germicidal irradiation) to more efficiently sterilize PPE.

### Conclusion

Cardiology is fertile ground for digital innovation, given its data-driven foundation and rapidly expanding digital footprint. ML and ER are 2 technologies at the forefront of these innovative efforts. Although their use in cardiology is still in its early stages, each is showing early promise. It is easy to envision a future state in which these 2 technologies are combined to yield exponential dividends to patients, physicians, and their teams.

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The authors report the following conflicts: ZA, FLJ, PF, SK, and SA have filed intellectual property related to the AI algorithms used in electrocardiogram interpretation; AL, MVZ,

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