Machine Learning Estimation of Myocardial Ischemia Severity Using Body Surface ECG

Rui Jin[1,3], Jake A Bergquist[1,2,3], Deekshith Dade[1], Brian Zenger[6], Xiangyang Ye[4], Ravi Ranjan[2,3,4], Rob S MacLeod[1,2,3], Benjamin A Steinberg[4], Tolga Tasdizen[1,5]

[1] Scientific Computing and Imaging Institute, University of Utah, SLC, UT, USA
[2] Nora Eccles Treadwell CVRTI, University of Utah, SLC, UT, USA
[3] Department of Biomedical Engineering, University of Utah, SLC, UT, USA
[4] School of Medicine, University of Utah, SLC, UT, USA
[5] Department of Electrical and Computer Engineering, University of Utah, SLC, UT, USA
[6] Department of Internal Medicine, Washington University in St Louis, St Louis, MO, USA

Abstract

Acute myocardial ischemia (AMI) is one of the leading causes of cardiovascular deaths around the globe. Yet, clinical early detection and patient risk stratification of AMI remain an unmet need, in part due to poor performance of traditional electrocardiogram (ECG) interpretation. Machine learning (ML) techniques have shown promise in analysis of ECGs, even detecting cardiac diseases not identifiable via traditional analysis. However, there has been limited usage of ML tools in the case of AMI due to a lack of high-quality training data, especially detailed ECG recordings throughout the evolution of ischemic events. In this study, we applied ML to predict the ischemic tissue volume directly from body surface ECGs in an AMI animal model. The developed ML networks performed favorably, with an average R^2 value of 0.932 suggesting a robust prediction. The study also provides insights on how to create and utilize ML tools to enhance clinical risk stratification of patients experiencing AMI.

1. Introduction

Acute myocardial ischemia (AMI) is one of the leading causes of sudden cardiac death worldwide.[1, 2] AMI results from an abrupt imbalance between cardiac metabolic demand and cardiac perfusion, leading to severe malfunctions of the heart.[3–5] There remains a critical yet unmet need for consistent, early, clinical detection and risk stratification of patients who might experience severe morbidity or even mortality due to AMI.[5] The task is fairly challenging, especially when patients show atypical symptoms of complete coronary obstruction, thereby calling for a more useful and clinically adaptable tool to facilitate better diagnoses and prognoses.

The electrocardiogram (ECG) is a noninvasive tool commonly used to diagnose and monitor AMI.[6] Even so, the use of ECG-based tools in risk stratification is limited, since clinical ECG diagnosis does not provide precise information about the size of ischemic regions in the heart.[7,8] On the other hand, machine learning (ML) techniques have been proven to be a useful and effective supportive tool to identify cardiac disorders otherwise undetectable in traditional ECG interpretation techniques.[9–11]

Contemporary application of ML in predicting cardiovascular diseases is limited, primarily due to the lack of high-resolution, controlled, and well-labeled training datasets.[12] Specifically, the limited sample size can introduce biases in the trained networks, making them more difficult to implement in broader clinical scenarios.[12] Large animal model data, however, may provide a viable avenue to develop such ML analytic tools, due to the detail, volume, and control in the data available from such models.[8]

In this study, we leverage a unique dataset of large animal experimental recordings of myocardial ischemic events to create robust ML tools for myocardial ischemia evaluation. We develop ML networks that can predict the size of the ischemic regions directly from the body surface ECG recordings. This study aims to demonstrate a step toward the improvement of ML-ECG tools for clinical risk stratification of AMI patients by leveraging animal data.

2. Methods

Dataset: Our dataset consisted of continuous recordings of controlled graded myocardial ischemia in a porcine

large animal model described in Zenger *et al.*[8, 13, 14] The dataset consisted of 8 replicates in which recordings were taken on the body surface and heart surface, as well as within intracardiac space during controlled episodes of ischemic stress. During ischemic interventions, the blood flow through the left anterior descending (LAD) coronary artery was controlled by a surgically implanted hydraulic occluder. Reversible transient ischemic stress was induced by a combination of LAD occlusion (up to 90%), and either atrial pacing or pharmacological stimulation via dobutamine. The recordings were made continuously and simultaneously across all electrodes at 1,000 Hz. Each experiment consisted of 3 to 9 individual ischemic interventions, as well as the corresponding baseline and recovery control recordings before and after each intervention. The signal recording and processing were completed by a suite of custom processing tools, hardware, and software.[8, 15]

The individual heartbeats from each experiment were isolated using PFEIFER, and resampled to 1,000 time steps[15]. Ischemic tissue volume was calculated using the transmural plunge needle recordings as described previously.[13] Briefly, needle geometry was acquired using postexperiment magnetic resonance imaging (MRI) processes. Then, for each heartbeat, the ST segment potentials were interpolated into this volume. The volume of tissues that had an ST segment deviation above 3 mV was considered ischemic, especially the value of ST40%, the measured voltage at 40% of the ST segment.[8] The ischemic volume is the gold standard that the ML-ECG models target to achieve (Figure 1).

In total, 79,714 data pairs of body surface potential (BSP) signal and ischemic volume were extracted across the 8 experiments. The data pairs were then randomly distributed into a 90%-10% training-validation split, where the training dataset had 71,743 data pairs and the validation dataset had 7,971 data pairs. The same training-validation split pattern was applied to all subsequent analyses.

Machine Learning Architecture and Training for ECG: The ischemic volumes were predicted using a regression training with a custom convolutional neural network similar to that described by Bergquist *et al.*[16,17] The network architecture was modified to have one spatial and one temporal resolution, with a 7x1 filter and an 1x5 filter, respectively. Additionally, a softplus was added to the output to ensure the target values stay positive.[16,17] The networks were trained with the mean squared error loss between the network predictions and the target ischemic volumes using the body surface ECGs as inputs, and the Adam optimizer was used to fine-tune the weights. Each network was trained for 50 iterations, where the training and validation R^2 values were monitored to evaluate network performance. Five replicates of training and validation steps were completed to minimize the effects of initialization.

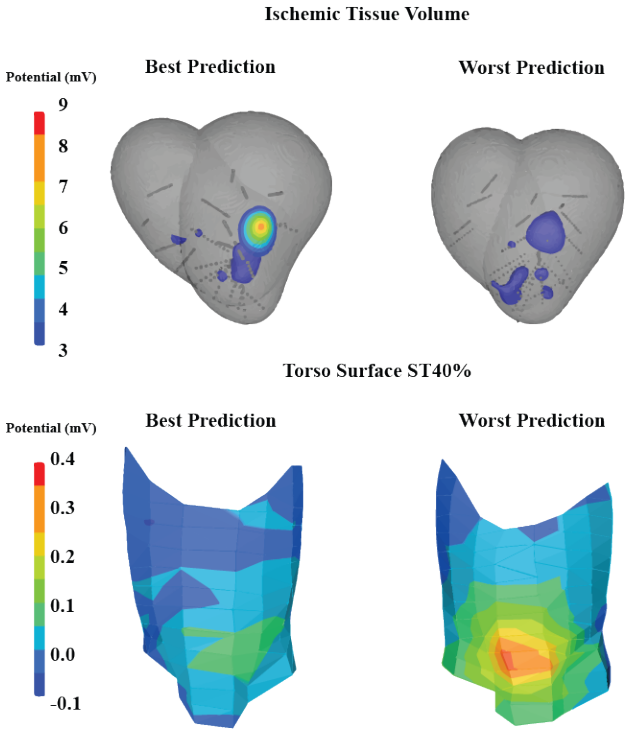

Figure 1. Sample Visualization of the input and output of the ML tools. The ML network predicts the ischemic tissue volumes (top) from the torso surface ECG recordings (bottom, ST40% values interpolated). The intracardiac needle electrodes recording the electrograms were visualized within the heart geometry (gray spheres). Based on the error of the specific prediction, the best (left) and worst (right) performing cases were found and the input-output pairs were visualized, respectively. The ST40% values of the best and worst performing heartbeat were used to visualize across the torso geometry. The best-performing model, network #3, was used here for demonstration purposes.

All machine learning was implemented using the Pytorch library.[18]

Analysis metrics: R^2 value (coefficient of determination) was used to evaluate network performance for both the training and testing sets[19]. In addition, the root mean square error (RMSE) was calculated for each of the 5 networks according to the following equation:

$$RMSE = \sqrt{\frac{\sum_{n=1}^{N}(\hat{r}_n - r_n)^2}{N}}, \quad (1)$$

where N is the sample size, $\hat{r}_n$ is each individual estimated value and r_n is the associated observed value.[20]

The validation dataset was also examined and categorized based on the size of the ischemic tissue. An ischemic region above 10 cm^3 was considered a large ischemic region, whereas a region below 10 cm^3 was considered a small or no ischemic region. Across the validation dataset (n = 7,971), 10.39% of the data were identified as having a large ischemic region (n = 828), and 89.61% of the data were identified as having a small or no ischemic region (n

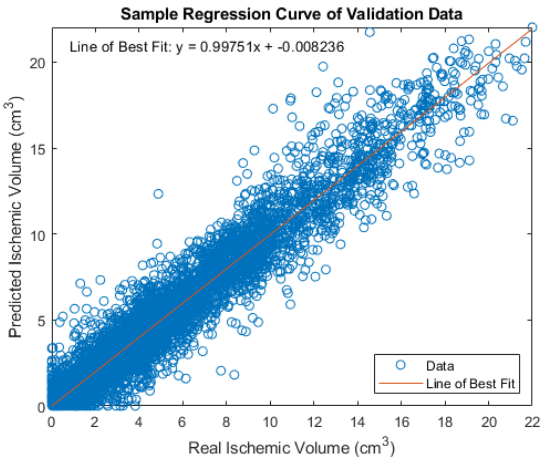

Figure 2. The sample regression curve of the network performance on validation data. The predicted volumes by the ML network were compared to the real volumes (blue circles, units of cm^3). A linear line of best fit was also visualized (orange). The best-performing model, network #3, was used here for demonstration purposes.

= 7,143). The RMSE values for both groups were calculated and contrasted to the overall average.

3. Results

Five networks were trained and evaluated on the ischemic volume dataset. Across all networks, the peak R^2 value for the validation dataset was found to be 0.937, and the average R^2 value was 0.932 ± 0.004 (Table 1).

Table 1. The R^2 and the RMSE values from the validation of the 5 ML networks

Network #	Validation R^2	RMSE (cm^3)
1	0.936	1.084
2	0.931	1.129
3	0.937	1.079
4	0.926	1.171
5	0.931	1.130
Mean	0.932	1.119
±Standard Deviation	±0.004	±0.034

The RMSE for each network was also calculated, with the smallest error being 1.079 cm^3 and the average being 1.119 ± 0.034 cm^3 (Table 1). In general, as the R^2 value increases, the RMSE decreases in line with the improved accuracy. The error can be more directly represented in a regression curve (Figure 2).

Among the large ischemic region data, the average RMSE across the 5 networks was found to be 1.900 ± 0.067 cm^3, which represented a 70% increase compared to the overall RMSE average. On the other hand, for data with small or no ischemic regions, the average RMSE was found to be 0.989 ± 0.035 cm^3, a 12% decrease compared to the overall RMSE average.

4. Discussion and Conclusions

In this study, 5 ML networks were trained on the same regression task to predict the ischemic tissue volumes on the simultaneously recorded body surface ECGs. The best-performing network achieved a validation R^2 value of 0.937, and all 5 networks achieved a validation R^2 value over 0.925. The average RMSE was 1.119 cm^3 across all networks, and no networks have an RMSE exceeding 1.180 cm^3. The high R^2 values and the low errors show that the networks have robust performances when predicting ischemic volumes directly from ECGs, a feature that traditional ECG interpretation does not allow.

When comparing the prediction accuracy across different ischemic sizes, the networks generally performed better for small to no ischemic regions, according to the decrease in the average RMSE. Such results may indicate that as the ischemic region size grows, the complexity of the signal and difficulty in predicting its volume also grow. The geography of the ischemic regions might also contribute to this behavior. Particularly, the ischemic regions usually localize to one territory in the heart, whereas the body surface ECG data records over all territories. The training dataset could also have more low ischemic volume data points, leading to the bias in the performance.

The performance of the networks in ischemic volume prediction suggests that the spatiotemporal design of the network is advantageous in learning the features contained in a multi-electrode ECG recording. Specifically, the design can incorporate the spatial correlations of the signals, due to their proximity in location, in addition to the temporal features of the ECG waveform. The discovery leads the way for an array of future applications of this network design. In addition to independent ECG analysis, the ML tools presented in this study can also be combined with electrocardiographic imaging (ECGI) techniques for localizing myocardial ischemia.[21] ECGI techniques can leverage knowledge of the torso anatomy, electrode locations, and electrical tissue conductivities, thus providing a higher spatial resolution in estimating the bioelectric sources in the heart than traditional 12-Lead ECGs.[21] Such combined physics-based (ECGI) and data-driven (ML) modeling may provide results superior to either alone.

One of the most substantial obstacles for ML network training is the lack of high-quality data. This lack is a problem especially when targeting human diseases, where the availability of detailed datasets is often limited. In this study, we leveraged a large animal model dataset to train ML networks. In the future, other ML approaches could benefit from training with animal datasets, and then pos-

sibly transitioning or transfer-learning to a human-specific yet limited dataset.

Future studies should include the application of these animal dataset-trained ML networks to various downstream tasks, such as other predictions within the animal dataset and possibly transitions to human datasets. Explainability analysis would help elucidate the mechanisms behind the ML-ECG analysis, given that myocardial ischemia produces a readily recognizable ECG signature. Furthermore, the datasets in this study included all the recordings across multiple varied ischemic interventions to represent a more diverse and representative cohort. However, the data can be further divided into preischemic and ischemic recordings, which may allow for more complicated ML tasks such as predicting ischemic response or outcome using preischemic signals. Such a risk-stratification ML tool that uses only preischemic ECG recordings would be helpful for clinical management. Lastly, the scope of this study was limited to predicting myocardial ischemic size only. Future applications of the same approach could expand to other clinical metrics of interest and create more useful tools for diagnosing and monitoring cardiac diseases.

Acknowledgments

Support for this research came from the Center for Integrative Biomedical Computing (www.sci.utah.edu/cibc), NIH/NIGMS grants P41 GM103545 and R24 GM136986, NIH/NIBIB grant U24EB029012, and the Nora Eccles Harrison Foundation for Cardiovascular Research.

References

[1] Murphy SL, Kochanek KD, Xu J, Arias E. Mortality in the United States, 2020. NCHS data brief 2021;(427):1–8. ISSN 1941-4927.

[2] Tsao CW, Aday AW, Almarzooq ZI, Anderson CA, Arora P, Avery CL, Baker-Smith CM, Beaton AZ, Boehme AK, Buxton AE, et al. Heart disease and stroke statistics—2023 update: a report from the American Heart Association. Circulation 2023;147(8):e93–e621.

[3] Amsterdam EA, Wenger NK, Brindis RG, Casey DE, Ganiats TG, Holmes DR, Jaffe AS, Jneid H, Kelly RF, Kontos MC, et al. 2014 AHA/ACC guideline for the management of patients with non–ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Journal of the American College of Cardiology 2014;64(24):e139–e228.

[4] Zenger B, Good WW, Bergquist J, Tate JD, Sharma V, MacLeod RS. Electrocardiographic comparison of dobutamine and bruce cardiac stress testing with high resolution mapping in experimental models. In 2018 Computing in Cardiology Conference (CinC), volume 45. IEEE, 2018; 1–4.

[5] Al-Khatib SM, Stevenson WG, Ackerman MJ, Bryant WJ, Callans DJ, Curtis AB, Deal BJ, Dickfeld T, Field ME, Fonarow GC, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Journal of the American College of Cardiology 2018;72(14):e91–e220.

[6] McCarthy BD, Wong JB, Selker HP. Detecting acute cardiac ischemia in the emergency department: a review of the literature. Journal of General Internal Medicine 1990; 5(4):365–373.

[7] Knuuti J, Ballo H, Juarez-Orozco LE, Saraste A, Kolh P, Rutjes AWS, Jüni P, Windecker S, Bax JJ, Wijns W. The performance of non-invasive tests to rule-in and rule-out significant coronary artery stenosis in patients with stable angina: a meta-analysis focused on post-test disease probability. European Heart Journal 2018;39(35):3322–3330.

[8] Zenger B, Good WW, Bergquist JA, Burton BM, Tate JD, Berkenbile L, Sharma V, MacLeod RS. Novel experimental model for studying the spatiotemporal electrical signature of acute myocardial ischemia: a translational platform. Physiological Measurement 2020;41(1):015002.

[9] Attia ZI, DeSimone CV, Dillon JJ, Sapir Y, Somers VK, Dugan JL, Bruce CJ, Ackerman MJ, Asirvatham SJ, Striemer BL, et al. Novel bloodless potassium determination using a signal-processed single-lead ECG. Journal of the American Heart Association 2016;5(1):e002746.

[10] Attia ZI, Sugrue A, Asirvatham SJ, Ackerman MJ, Kapa S, Friedman PA, Noseworthy PA. Noninvasive assessment of dofetilide plasma concentration using a deep learning (neural network) analysis of the surface electrocardiogram: a proof of concept study. PLoS One 2018;13(8):e0201059.

[11] Grogan M, Lopez-Jimenez F, Cohen-Shelly M, Dispenzieri A, Attia ZI, Abou Ezzedine OF, Lin G, Kapa S, Borgeson DD, Friedman PA, et al. Artificial intelligence–enhanced electrocardiogram for the early detection of cardiac amyloidosis. In Mayo Clinic Proceedings, volume 96. Elsevier, 2021; 2768–2778.

[12] Cai YQ, Gong DX, Tang LY, Cai Y, Li HJ, Jing TC, Gong M, Hu W, Zhang ZW, Zhang X, et al. Pitfalls in Developing Machine Learning Models for Predicting Cardiovascular Diseases: Challenge and Solutions. Journal of Medical Internet Research 2024;26:e47645.

[13] Zenger B, Good WW, Bergquist JA, Rupp LC, Perez M, Stoddard GJ, Sharma V, MacLeod RS. Pharmacological and simulated exercise cardiac stress tests produce different ischemic signatures in high-resolution experimental mapping studies. Journal of Electrocardiology 2021;68:56–64.

[14] Zenger B, Good WW, Bergquist JA, Rupp LC, Perez M, Stoddard GJ, Sharma V, MacLeod RS. Transient recovery of epicardial and torso ST-segment ischemic signals during cardiac stress tests: A possible physiological mechanism. Journal of Electrocardiology 2021;69:38–44.

[15] Rodenhauser A, Good WW, Zenger B, Tate J, Aras K, Burton B, MacLeod RS. PFEIFER: Preprocessing framework for electrograms intermittently fiducialized from experimental recordings. Journal of Open Source Software 2018;3(21):472.

[16] Bergquist JA, Zenger B, Brundage J, MacLeod RS, Shah R, Ye X, Lyones A, Ranjan R, Tasdizen T, Bunch TJ, et al. Comparison of Machine Learning Detection of Low Left Ventricular Ejection Fraction Using Individual ECG Leads. In 2023 Computing in Cardiology (CinC), volume 50. IEEE, 2023; 1–4.

[17] Bergquist JA, Zenger B, Brundage J, MacLeod RS, Bunch TJ, Shah R, Ye X, Lyons A, Ranjan R, Tasdizen T, et al. Performance of Off-the-Shelf Machine Learning Architectures and Biases in Detection of Low Left Ventricular Ejection Fraction. medRxiv 2023;2023–06.

[18] Paszke A, Gross S, Massa F, Lerer A, Bradbury J, Chanan G, Killeen T, Lin Z, Gimelshein N, Antiga L, et al. Pytorch: An imperative style, high-performance deep learning library. Advances in Neural Information Processing Systems 2019;32.

[19] Dodge Y. Coefficient of Determination. New York, NY: Springer New York. ISBN 978-0-387-32833-1, 2008; 88–91.

[20] Wang W, Lu Y. Analysis of the mean absolute error (MAE) and the root mean square error (RMSE) in assessing rounding model. In IOP Conference Series: Materials Science and Engineering, volume 324. IOP Publishing, 2018; 012049.

[21] Bergquist J, Rupp L, Zenger B, Brundage J, Busatto A, MacLeod RS. Body surface potential mapping: contemporary applications and future perspectives. Hearts 2021; 2(4):514–542.

Address for correspondence:

Rui Jin
University of Utah
72 Central Campus Dr, Salt Lake City, UT 84112
rui.jin@utah.edu