12-Lead ECG Reconstruction via Combinatoric Inclusion of Fewer Standard ECG Leads with Implications for Lead Information and Significance

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Keywords: ECG, Limited Lead Systems, ECG Synthesis, ECG Reconstruction.

Abstract: The electrocardiogram (ECG) is the most widely used, non-invasive, cardiovascular test. There exist many lead variations including a one, three, six, and 12-lead device. In this work, we use ECGio, a validated deep learning model for the assessment of coronary artery disease, to reconstruct ECG signals with various combinations of leads, ranging from a single lead, to the full 12-leads. We are able to show 0.6536 R^2, and 0.0747 mean absolute error (MAE) in the accurate reconstruction of a full 12-lead signal from just lead II. We go one step further and look at which individual leads, and in what combinations, yield the most accurate reconstructions as measured by R^2 and MAE. As you would expect, the larger the quantity of leads included, the more accurate the reconstruction. Overall, the mean performance across all possible lead combinations is 0.8335 R^2, and 0.0538 MAE. This work opens the door for seeing if ECGio can handle systematic noise injection and missing or misplaced leads.

1 INTRODUCTION

First introduced in the late 1800s, the electrocardiogram (ECG) is the most widely used, non-invasive, cardiovascular test (AlGhatrif and Lindsay, 2012). The ECG measures voltage generated in the heart as it depolarizes and repolarizes by recording the potential difference on the body's surface. As it was adopted clinically, ECG patterns were correlated with various arrhythmias and cardiac conditions, often before the underlying physiological mechanism was elucidated (Yang et al., 2015). Currently, the ECG is an early-stage diagnostic test, serving to identify and preliminarily quantify myocardial infarctions (MI) (Members et al., 2013), ischemia (Fihn et al., 2014), and rhythm disorders such as atrial (January et al., 2014) and ventricular tachycardias (Al-Khatib et al., 2018).

The most common ECG is a 12-lead although one, three, and six lead devices are still in use. In the standard 12-lead ECG, there are ten different electrodes (three limb and six chest leads and one electrode going to ground) that also generate three augmented leads via linear combination of the limb and chest leads. The names and are shown in Table 1. Besides the number of leads, a multitude of lead placements exist offering different trade-offs between lead placement/number verse patient comfort and physicians' ability to consistently and accurately place those additional, nontraditional leads (Chou, 1986). The most popular nontraditional lead placement configurations include, but are not limited to, Frank's Lead system (Frank, 1956), and the four EASI electrode system (Dower et al., 1988).

Additionally, devices such as the Holter Monitor, Zio Patch [1], AliveCor KardiaMoblie [2], and Apple

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Jain, U., Butchy, A., Leasure, M., Covalesky, V., Mccormick, D. and Mintz, G.
12-Lead ECG Reconstruction via Combinatoric Inclusion of Fewer Standard ECG Leads with Implications for Lead Information and Significance.
DOI: 10.5220/0010788600003123
In *Proceedings of the 15th International Joint Conference on Biomedical Engineering Systems and Technologies (BIOSTEC 2022) - Volume 4: BIOSIGNALS*, pages 133-141
ISBN: 978-989-758-552-4; ISSN: 2184-4305

Table 1: The 12 leads, the location of the positive and negative electrodes, and which heart surface they are thought to represent. "N" refers to neutral or electric ground.

Lead	+ Location	- Location	Surface
I	Left Arm	Right Arm	Lateral
II	Left Leg	Right Arm	Inferior
III	Left Leg	Left Arm	Inferior
aVR	Right Arm	N	None
aVL	Left Arm	N	Lateral
aVF	Left Leg	N	Inferior
V1	Right side of sternum, 4th intercostal space	N	Septum
V2	Left side of sternum, 4th intercostal space	N	Septum
V3	Between V2 & V4	N	Anterior
V4	Left midclavicular line, 5th intercostal place	N	Anterior
V5	Left anterior axillary line	N	Lateral
V6	Left midaxillary line	N	Lateral

Watch [3] offer a varying number of leads and alternative lead placements, but still aim to capture signals that are similar to the common 12-lead ECG.

Devices that employ fewer leads typically have less chance of misplaced leads, but contain less information. Thus, there are many methods and algorithms to convert and/or reconstruct signals collected from one device into another device (Finlay et al., 2007).

Until recently, the most common methods to reconstruct a 12-lead signal using fewer than the standard 12-leads was either linear regression (Trobec and Tomašić, 2011) (Tomašić and Trobec, 2013a) (Zhu et al., 2018) or through a principal component analysis (Dawson et al., 2009) (Mann and Orglmeister, 2013). Within the last decade, there has been a tremendous push in the field of machine learning and artificial intelligence to tackle this problem.

(Grande-Fidalgo et al., 2021) employed ANN to reconstruct 12-lead ECG from a proprietary three-lead device in 7 people. (Smith et al., 2021) created a focus time-delay neural network (FTDNN) using 7 leads to derive the remaining 5 precordial leads (V1, V3-V6). (Sohn et al., 2020a) created a long short-term memory (LSTM) network to overcome the issue of reduced horizontal components of the vector in the electric signal obtained from the patch-type device attached to the anterior chest.

For a more rigorous review of ECG reconstruction methods, please refer to (Trobec et al., 2018) and (Tomašić and Trobec, 2013b). The assumption underlying these attempts was that the information used to make clinical decisions from a 12-lead ECG was also present and extractable from a system with fewer leads.

Heart Input Output, Inc. (DBA HEARTio) has developed a novel deep learning algorithm that reconstructs a 12 lead ECG from missing leads. Our algorithm, ECGio, was developed to screen patients for coronary artery disease (CAD, the cause of most rhythm disorders and acute events) and has been validated in 1,659 patients as verified by coronary angiography (Leasure et al., 2021). This paper's novel contribution to lead reconstruction describes, ECGio's ability to take any number and/or combination of leads and reconstruct an accurate representation of the original 12-lead signal. For example, ECGio can recreate a full 12-lead utilizing only Lead I and lead aVR from a non-standard ECG recording device. In addition, ECGio is not limited to only 12-lead reconstruction, but can do a multitude of transformations (i.e. 12 lead to 128 leads, etc.). As a deep learning architecture, ECGio will continue to improve.

In this this paper. we demonstrate ECGio's ability to accurately reconstruct a 12-lead ECG from a single lead (any of the standard 12-leads). Next we use combinations of leads to reconstruct the 12-lead ECG. Finally, we look at ECGio's ability to reconstruct a 12-lead ECG and determine which leads were most useful for faithful reconstruction

2 METHODS

2.1 Data Source

This is a study proof-of-concept study into the ability of a deep learning model (ECGio) to reconstruct missing ECG information. There were 3 distinct experiments done on 250 randomly selected patients from PTB-XL, a large publicly available electrocardiography dataset (Wagner et al., 2020). Only 250 patients were used as a test set because of the high degree of computation involved in the experiments although other similar works have used fewer ECGs (Sohn et al., 2020b). Overall, **1,023,750** different ECG input combinations were constructed from the original 250 patients.

2.2 Data Standardization

We standardized the ECG signal in-put being sent to the deep learning model. Each ECG signal was clipped such that it represented one second of ECG time and in the form $N \times M$, where M was the number of leads and N the number of samples. Since each signal was only one second in length, N was also equal to the sampling rate. Using Fast Fourier Transform (FFT), we resampled the signal to reduce the sampling rate to 100Hz. To make sure only the infor-

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mation within this band of frequencies was retained while others were removed, we used a Bandpass Butterworth filter with passband starting at 2Hz and extending to 40Hz.

The databased ECG signals were recorded in millivolts (mV), with irregular maxima and minimum values. To conform to best machine learning practices, we scaled each one second ECG segment to values between [-1. +1] using Equation 1 as is common in deep learning to standardize input signals:

$$f(x) = 2\frac{x - min(x)}{max(x) - min(x)} - 1 \quad (1)$$

where x represented an ECG array as recorded in millivolts (mV), max(x) the maximum value along x, and min(x) the minimum value along x. Any null values were converted to zeros. Eventually each signal was detrended such that the isoelectric portions of the ECG were equal to zero.

The 12-lead standardized data was the reference when performance metrics were calculated. We did not use raw voltage difference values as the reference similar to Sohn et al., (Sohn et al., 2020b) to avoid a large potential variance in the existence of muscle, movement, or electric noise causing deviations from signal to signal. Standardized signals would bring a more fair comparison mathematically whereas a straight comparison of performance metrics between our results and others might not be prudent.

2.3 Experiments & Goals

There were three different experiments:

1. **1 Lead Reconstruction:** Can ECGio use 1 lead of ECG information to accurately and faithfully reconstruct a 12 lead ECG? If so, which single lead resulted in the highest performance?
2. **Multi-lead Reconstruction:** Can ECGio use different ECG lead combinations to accurately and faithfully reconstruct a 12 lead ECG? If so, what was the correlation between the number of leads used as input and performance?
3. **Lead Significance:** Did the inclusion or exclusion of specific leads affect performance?

2.4 Performance Metrics

In all three experiments there were two key performance metrics: mean absolute error (MAE) and the Pearson correlation coefficient (R^2). For each of these values, we calculated the mean (μ) and the standard deviation (σ) similar to other studies. Furthermore, these metrics were calculated easily and were easy to interpret.

MAE was defined as:

$$MAE(y,\hat{y}) = \frac{1}{N}\sum_{i=1}^{N}|y_i - \hat{y}_i| \quad (2)$$

where y is the ground truth and $\hat{y}$ is the predicted value. Each element of the 12-lead ECG array is used for the purposes of this mean with no difference in weighting among the leads.

R^2 is defined as:

$$R^2(y,\hat{y}) = \frac{\mathbb{E}[(y-\mu_y)(\hat{y}-\mu_{\hat{y}})]}{\sigma_y\sigma_{\hat{y}}} \quad (3)$$

where y is the ground truth and the $\hat{y}$ is the predicted value. Each element of the 12-lead ECG array is used for the purposes of this mean with no difference in weighting among the leads. $\mathbb{E}$ is used to indicate expectation, μ is the mean, and σ is the standard deviation.

2.5 1 Lead Reconstruction

We used a previously-trained model of ECGio where the input was an ECG in matrix format, and our output of interest was an ECG in matrix format (Leasure et al., 2021)). Although ECGio has many outputs, in this paper only this reconstruction output was used. As detailed in the methodology, the population of 250 ECGs from the PTB-XL database was standardized before reconstruction. Each was inputted into ECGio 12 separate times, each time using a different single lead of information while the remaining eleven leads were masked to zero. Each time an ECG was inputted, a unique lead index assured that each individual lead was used once. After the input was propagated, the reconstructed ECG was collected and stored.

2.6 Multi-lead Reconstruction

To determine the effect of lead number and significance, different leads were systematically included or removed from the same 250 patient set. All possible combinations of lead inclusion were explored for each patient.

In this situation we let $S = \{1,2,3,...,11,12\}$. Let S_k represent a set of all the combinations of S with k length combinations. Then let A represent the set that is the union of all the combinations, $A = \{S_1, S_2, S_3, ..., S_{10}, S_{11}, S_{12}\}$. Each set in A indicated which leads in the input ECG should remain intact and all others were masked to zero. Performance statistics were averaged across each S_k. In Table 2 combinations for each different S_k and the total number of combinations done for the 250 ECG population are shown.

Table 2: All the possible lead combinations for just one patient's ECG. The Total Combinations row results from multiplying the number of combinations for one ECG with the total number of patients in the whole population (250).

# of Leads	# of Combinations
1	12
2	66
3	220
4	495
5	792
6	924
7	792
8	495
9	220
10	66
11	12
12	1
Sum	4,095
Total Combinations	**1,023,750**

2.7 Lead Significance

Based on the analyses performed above, we determined which leads, when included or excluded, lead to a statistically significant change in performance by taking every combination $c \in A$ and determining which leads were included and which were excluded. For example, if $c_0 = \{1,2,3\}$, then leads 1, 2, 3 were included and the rest were excluded. When testing the statistical significance of lead 1, c_0 would be used for the inclusion of lead 1, while any combination that did not contain lead 1 would be excluded. It would be the opposite scenario if it were leads 4-12.

This exercise was followed for every combination in A until we had 24 subsets with each lead having 2 corresponding subsets indicating whether the lead was or was not included. For each pair of subsets, performance metrics were calculated and a p-value calculated in order to determine if the difference between the distribution of the performance metrics was statistically significant.

3 RESULTS

3.1 1 Lead Reconstruction

The MAE and R^2 were calculated for each patient's ECG reconstruction using just one lead. These values were averaged across all 250 patients to obtain the mean and standard deviations reported in Table 3.

Table 3: The MAE and R^2 mean and standard deviation across the whole patient population of ECG reconstruction from just one lead. The first column includes which lead was used for the reconstruction.

Lead	MAE μ	MAE σ	R^2 μ	R^2 σ
I	0.0755	0.0238	0.6498	0.1914
II	0.0747	0.0274	0.6536	0.2172
III	0.0836	0.0280	0.6003	0.2215
aVR	0.0775	0.0280	0.6225	0.1986
aVL	0.0814	0.0279	0.6169	0.2105
aVF	0.0788	0.0270	0.6281	0.2020
V1	0.0834	0.0273	0.5734	0.2013
V2	0.0818	0.0258	0.5786	0.2117
V3	0.0792	0.0252	0.5952	0.1975
V4	0.0775	0.0248	0.6141	0.1971
V5	0.0757	0.0265	0.6317	0.2102
V6	0.0757	0.0261	0.6374	0.2026

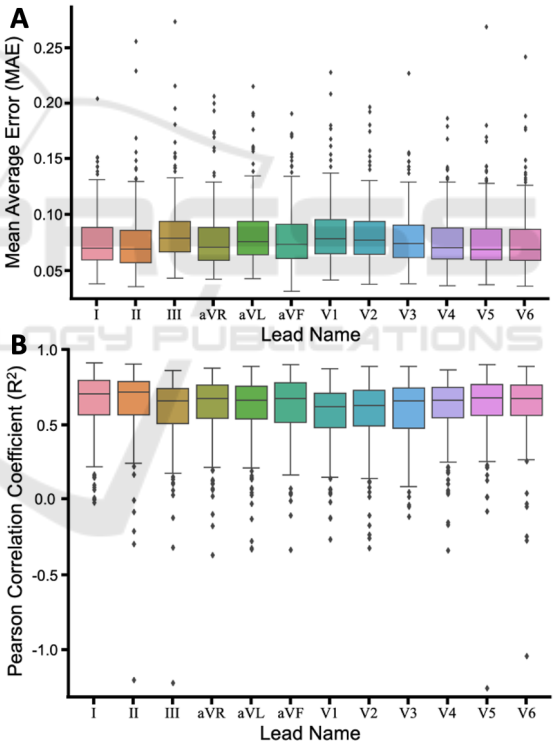

Figure 1: The (A) MAE and (B) R^2 of all patients using a particular lead. Outliers are shown as black diamonds.

To illustrate the spread in reconstruction fidelity within the population, Figure 1 shows two measures of reconstruction fidelity as box and whisker plots, with outliers indicated as black diamonds.

We did not observe a huge deviation in reconstruction depending upon which lead was used. This points

to one lead including sufficient information to reconstruct a full 12-lead set. The mean best performance was observed using lead II and the worst was with lead III with a range of 0.0747 - 0.0836 for MAE, and 0.6003 and 0.6536 for R^2. Quite a few outliers were observed and responsible for lowering the reconstruction fidelity. The overall individual highest performing ECG was with a MAE of 0.0321 and a R^2 of 0.964, with surprisingly only six leads selected for input.

3.2 Multi-lead Reconstruction

In total, 1,023,750 different combinations were created across all 250 patients. Reconstructions were compared against the full, true patient 12-lead ECG to calculate performance metrics. In Table 4, we report the mean MAE and R^2 metrics of reconstruction fidelity, grouping the number of leads that went into the reconstruction. To illustrate the spread in reconstruction fidelity based on the number of leads, Figure 2 shows two measures of reconstruction fidelity as box and whisker plots, with outliers indicated as black diamonds.

Table 4: The MAE and R^2 mean and standard deviation across the whole patient population for ECG reconstructions using different combinations of leads. For example, in 2 leads, we report the performance of any reconstruction that used any 2 lead combination for reconstruction.

#	MAE μ	MAE σ	R^2 μ	R^2 σ
1	0.0787	0.0267	0.6168	0.2068
2	0.0684	0.0226	0.7127	0.1574
3	0.0623	0.0199	0.7662	0.1268
4	0.0582	0.0181	0.8005	0.1056
5	0.0552	0.0169	0.8243	0.0911
6	0.0529	0.0161	0.8415	0.0811
7	0.0512	0.0155	0.8539	0.0741
8	0.0499	0.0151	0.8629	0.0692
9	0.0490	0.0147	0.8694	0.0659
10	0.0483	0.0145	0.8743	0.0636
11	0.0477	0.0144	0.8779	0.0621
12	0.0474	0.0143	0.8806	0.0609

Overall and as expected, there was a consistent increase in performance when more leads were included. The best performing number of leads was twelve and the worst performing was one with a range of 0.0474 - 0.0787 for MAE, and 0.6168 - 0.8806 for R^2. There was also a decrease in the maximum negative range as more leads were inputted.

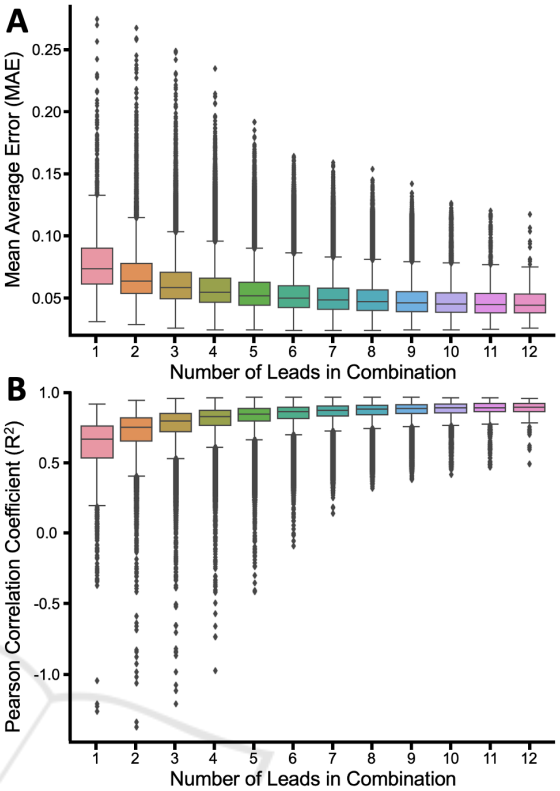

Figure 2: The (A) MAE and (B) R^2 of all patients using a particular number of leads in combination. Outliers are shown as black diamonds.

3.3 Lead Significance

Finally, performance statistics were calculated for various groups of leads depending on whether or not the reconstruction used a specific lead or combination of leads. Table 5 reports the MAE and R^2 values when specific leads were included and sent to EC-Gio and when they were excluded. These groups included reconstructions that used just one lead, up to the full 12-leads, to identify which leads could significantly alter reconstruction fidelity. P-values were calculated by comparing the performance when the lead was included against the performance of all reconstructions when it was excluded. We calculated p-values for both MAE and R^2 performance metrics, and these values are reported in Table 6. Leads I, II, III, aVL, aVF, V2, and V3 all had significant difference (p-value <0.05) between reconstructions that included these leads from those reconstructions that excluded these leads.

Table 5: The mean and standard deviations of performance statistics (MAE and R^2) reported for all combinations of leads, grouped based on which leads are included (with) and excluded (without). For example, the average MAE is reported for all reconstructions that used Lead II in "With Lead" and all reconstructions that didn't use Lead II in "Without Lead".

Lead	MAE				R^2			
	With Lead		Without Lead		With Lead		Without Lead	
	μ	σ	μ	σ	μ	σ	μ	σ
I	0.053	0.017	0.055	0.018	0.842	0.085	0.825	0.102
II	0.053	0.017	0.055	0.018	0.842	0.086	0.825	0.101
III	0.053	0.017	0.055	0.018	0.843	0.085	0.824	0.101
aVR	0.053	0.017	0.055	0.017	0.839	0.089	0.828	0.099
aVL	0.053	0.017	0.055	0.018	0.845	0.084	0.822	0.102
aVF	0.053	0.016	0.055	0.018	0.845	0.083	0.822	0.102
V1	0.053	0.017	0.055	0.018	0.841	0.086	0.826	0.100
V2	0.052	0.016	0.055	0.018	0.843	0.086	0.824	0.101
V3	0.052	0.016	0.055	0.018	0.844	0.086	0.823	0.100
V4	0.053	0.016	0.055	0.018	0.842	0.088	0.825	0.099
V5	0.053	0.016	0.055	0.018	0.840	0.089	0.827	0.099
V6	0.053	0.017	0.055	0.018	0.839	0.089	0.828	0.099

Table 6: Table reporting the p-values associated with the level of significance between the performance of the ECG reconstructions that included (with) or excluded (without) that particular lead. Both p-values are reported for MAE and R^2. Leads with R^2 p-values <0.05 are denoted with an asterisk.

Lead	p-value	
	MAE	R^2
I*	0.176	0.039
II*	0.157	0.049
III*	0.301	0.030
aVR	0.299	0.194
aVL*	0.159	0.008
aVF*	0.117	0.006
V1	0.136	0.062
V2*	0.050	0.018
V3*	0.041	0.009
V4	0.096	0.052
V5	0.163	0.111
V6	0.228	0.170

4 DISCUSSION

The purpose of this study was to determine whether ECGio, a novel deep learning platform of HEARTio, could reconstruct a full 12-lead ECG from one or more leads. We used the mean absolute error (MAE) and the Pearson correlation coefficient (R^2) which are standard performance metrics to measure ECG reconstruction fidelity. Both measures were calculated by comparing ECGio's reconstruction to the normalized ECG (as described in the methodology section). The normalization process does remove the amplitude information from the signal, which can impact the physiological importance of the ECG (i.e. certain conditions where the definition is dependent on an amplitude value). However, this doesn't affect the many pathologies where the qualitative features of the ECG matter more than the amplitude.

An example of ECGio reconstruction is shown in Figure 3, and demonstrates that complete correlation may not be possible because some noise still exists within the reference standard ECG and will not be seen in the reconstruction. This can be illustrated quantitatively, where despite there being a high visual match between the original and reconstructed ECG, the R^2 is not near 1. This noise is usually signal artifacts that result from issues with baseline recording or our filtering, and as signal noise in the middle of the signal.

In the first experiment we used only one lead of information to create a 12-lead ECG. This experiment yielded moderate correlation between the reference standard ECG and the reconstructed ECG. This level of correlation might offer clinicians additional information when dealing with limited technology (e.g. a one-lead patch or even a one-lead smartwatch ECG). Lead II performed best. A possible hypothesis was that a limb lead was harder to recreate than a precordial lead or that information from a limb lead can be used to recreate precordial leads and not vise-versa. It was also possible that this behavior was only extant within this 250 ECG dataset and not in an extended population.

In the second experiment, a higher level of reconstruction was exhibited with more information provided within the input ECG. The correlation increased

Table 7: This table showcases a sampling of other methods that are used in 12-lead ECG reconstruction. Note that the value used for R^2 for this work is for the mean value for associated lead subset.

Ref	Method	Sample Size	Lead Subset	R^2
(Trobec and Tomašić, 2011)	Linear Regression	65	2,3,4 lead subsets	0.954
(Zhu et al., 2018)	Linear Regression	39	I, II, V2	0.947
(Dawson et al., 2009)	Linear Affine Transformation	448	3-lead VCG	0.819
(Mann and Orglmeister, 2013)	Principal Component Analysis	24	6,9,11 lead subsets	0.950
(Grande-Fidalgo et al., 2021)	Artificial Neural Network	7	3 leads	0.997
(Smith et al., 2021)	Focus Time-Delay Neural Network	25	I, II, III aVL, aVR aVF, V2	0.861 - 0.968
(Sohn et al., 2020a)	LSTM Network	60	3 lead patch	0.95
This Work	Multi-output Deep Learning Model (ECGio)	250	Every combination	0.835
This Work	Multi-output Deep Learning Model (ECGio)	250	3 leads	0.762
This Work	Multi-output Deep Learning Model (ECGio)	250	6 leads	0.842
This Work	Multi-output Deep Learning Model (ECGio)	250	9 leads	0.869

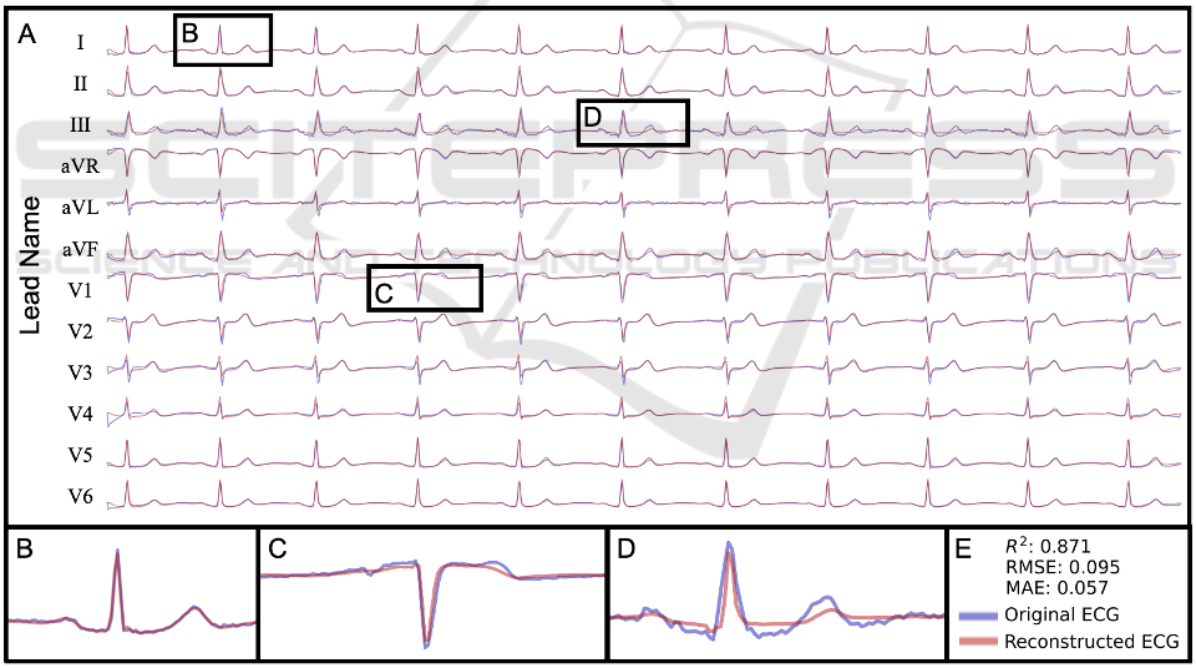

Figure 3: (a) An ECG reconstructed by ECGio (in semi-transparent red) using only lead I and compared against the true, original 12-lead ECG signal (in semi-transparent blue). (B) Enlarged lead I demonstrating that even though ECGio is given lead 1, it performs corrections and approximations in an attempt to correct for noise in the input signal. (C) Enlarged lead V1 demonstrating ECGio's reconstruction ability on an important precordial lead. (D) Enlarged lead III demonstrating ECGio's reconstruction ability on a noisy limb lead. This points to areas for improvement in future work. (E) Figure legend and performance statistics (R^2, Root Mean Square Error (RMSE) and MAE) for this particular one-lead reconstruction.

from moderate with 1 lead to high with 12-leads. This type of behavior was expected especially for clinicians who would prefer a more authentic reconstruction.

In the final experiment there were particular leads that were more significant in ECGio's ability to reconstruct a full 12-lead ECG. Either ECGio weighed information from some leads more highly than others,

or some leads contained more information and were therefore more significant to understanding a full 12-lead morphology. From the tests of significance, leads I,II, aVL, aVF, V2, and V3 – the majority of which were limb leads – were statistically significant. The unipolar leads aVL and aVF were linear combinations of limb leads and therefore their inclusion was also significant. V2 and V3 were also statistically significant and might be more important than other precordial leads. Again, this behavior might represent a larger trend or might be limited to this dataset.

In Table 7, we compared our results against a sampling of other methods with R^2 as the metric of comparison. At first glance, our work contained a lower R2 than others, but a few factors should be considered. (1) Our reference standard had the propensity to filtering artifacts as a result of standardization. (2) This work was a generalized model that used any combination of ECG leads and so that a decrease of performance in favor of flexibility was expected. (3) We limited the length of time to 10 seconds and we artificially lowered the sampling rate to 100Hz, which meant that there were less values in flat areas, such as isoelectric portions.

We also showed the potential of ECGio to be used to reconstruct a full 12-lead ECG when leads were either missing or unable to be collected. We also showed that there were leads of an ECG that may contain more information than others, namely the limb leads. In future studies, ECGio's scale, usability, and clinical viability must be examined. We must determine if results scale and if they demonstrate a larger trend in how ECG information is stored. The next step must include a larger sample size with the potential to capture the variance of ECGs. We need to show if the information provided by this reconstruction matches-up not only mathematically, but clinically. A future study should compare the reference standard ECG to the reconstruction in terms of clinical information delivered to physicians. In addition, the presence of abnormal beats and rhythms must be examined to determine if abnormal morphology affects ECGio's reconstruction capabilities.

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