Journal of Electrocardiology 52 (2019) 88–95

Contents lists available at ScienceDirect

Journal of Electrocardiology

journal homepage: www.jecgonline.com

# A deep neural network learning algorithm outperforms a conventional algorithm for emergency department electrocardiogram interpretation

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ARTICLE INFO

*Keywords:*
Electrocardiography
Computer
Deep neural network
Artificial intelligence
Big data

ABSTRACT

*Background:* Cardiologs® has developed the first electrocardiogram (ECG) algorithm that uses a deep neural network (DNN) for full 12-lead ECG analysis, including rhythm, QRS and ST-T-U waves. We compared the accuracy of the first version of Cardiologs® DNN algorithm to the Mortara/Veritas® conventional algorithm in emergency department (ED) ECGs.

*Methods:* Individual ECG diagnoses were prospectively mapped to one of 16 pre-specified groups of ECG diagnoses, which were further classified as "major" ECG abnormality or not. Automated interpretations were compared to blinded experts'. The primary outcome was the performance of the algorithms in finding at least one "major" abnormality. The secondary outcome was the proportion of all ECGs for which all groups were identified, with no false negative or false positive groups ("accurate ECG interpretation"). Additionally, we measured sensitivity and positive predictive value (PPV) for any abnormal group.

*Results:* Cardiologs® vs. Veritas® accuracy for finding a major abnormality was 92.2% vs. 87.2% ($p < 0.0001$), with comparable sensitivity (88.7% vs. 92.0%, $p = 0.086$), improved specificity (94.0% vs. 84.7%, $p < 0.0001$) and improved positive predictive value (PPV 88.2% vs. 75.4%, $p < 0.0001$). Cardiologs® had accurate ECG interpretation for 72.0% (95% CI: 69.6–74.2) of ECGs vs. 59.8% (57.3–62.3) for Veritas® ($P < 0.0001$). Sensitivity for any abnormal group for Cardiologs® and Veritas®, respectively, was 69.6% (95CI 66.7–72.3) vs. 68.3% (95CI 65.3–71.1) (NS). Positive Predictive Value was 74.0% (71.1–76.7) for Cardiologs® vs. 56.5% (53.7–59.3) for Veritas® ($P < 0.0001$).

*Conclusion:* Cardiologs' DNN was more accurate and specific in identifying ECGs with at least one major abnormal group. It had a significantly higher rate of accurate ECG interpretation, with similar sensitivity and higher PPV.



## Introduction

Computer electrocardiogram (ECG) interpretation algorithms aim to improve physician ECG interpretation, reduce medical error, and expedite patient care. Interpretations include both rhythm analysis and QRS-T-U analysis. Rapid interpretation is particularly important in the emergency department (ED), and although critical care and emergency physicians must be experienced in ECG interpretation, improved accuracy of automated interpretations could improve efficiency and patient safety [1,2]. However, computer algorithms have had mediocre performance [2]. Recent algorithms were only approximately 65% sensitive and 90% specific for ST Elevation Myocardial Infarction [3,4]. Furthermore, erroneous automated interpretations are associated with erroneous physician overreads, whereas accurate interpretations are associated with accurate physician overreads [5–7]. When ECGs are over-read by cardiologists, the presence of an automated interpretation results in lower accuracy, as the automated errors are frequently not corrected [8]. Erroneous computerized interpretations of atrial fibrillation, or its absence, have been correlated with erroneous final overreads, which adversely affected management [7]. Thus, an initial correct automated interpretation importantly influences the

*Abbreviations:* ECG, electrocardiogram; BBB, bundle branch block; STEMI, ST Elevation Myocardial Infarction; Non-STEMI, Non ST Elevation Myocardial Infarction; HR, heart rate; ED, emergency department; DNN, deep neural network; PPV, positive predictive value; NPV, negative predictive value; AV, atrio-ventricular.

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https://doi.org/10.1016/j.jelectrocard.2018.11.013
0022-0736/

final interpretation and, consequently, patient management. In spite of the importance and ubiquity of computer ECG interpretation, we are unaware of any publication of a direct comparative evaluation of any of the many algorithms in use; recent reviews made the same observation and also call for action to improve computerized ECG interpretation [2,9].

Deep Neural Network (DNN) machine learning algorithms use large amounts of data to "train" the computer by labeling each case according to one of many predefined abnormalities, allowing the computer to discern what characteristics of ECGs are associated with any given abnormality. A great advantage to DNN is they keep learning: the quality and accuracy is continuously refined as more data with outcomes or corresponding accurate interpretations accumulate. Unlike expert humans, who may retire or die, the DNN can continue to learn indefinitely. Eric Topol lists deep neural network learning application to skin cancer, as reported in Nature [10], as third among the top ten technological advances in medicine in 2017 [11].

DNN have been shown to be accurate for isolated labels of the ECG, such as rhythm diagnosis, in which it exceeded cardiologists' performance for arrhythmia detection [12]. However, Cardiologs Technologies has produced a new DNN algorithm (20 M parameters, 1.6 M neurons, 16 layers) which is not limited to interpretation of any one ECG label, but rather, for the first time, interprets the entire 12-lead ECG, including rhythm and QRS-T-U waves. The Cardiologs' DNN has already been shown to perform better than existing solutions, including Veritas®, at detecting atrial fibrillation [13,14]. The goal of this study is to assess the performance of this algorithm in the context of an ED, and with a larger scope of pathologies.

By the start of this study, this new Cardiologs Technologies DNN, had been trained on approximately 130,000 ECGs which were annotated by expert interpreters, with analysis of both conduction and the QRS-T-U waves. Training ECGs were recorded at multiple institutions, including at Hennepin County Medical Center (HCMC) in Minneapolis, MN, USA, from January 2013 through June 2016. The result is a function which takes an ECG as input and provides the probabilities of the presence of a list of abnormalities as output, producing a full rhythm and QRS-T-U analysis. This computation is performed using a sequence of simple operations such as matrix products. The coefficients of these matrices are however not directly interpretable, such that the internal workings of the algorithm are very difficult to decipher.

We sought to evaluate the performance of the first version of this new algorithm in a context where Cardiologs' solution is typically used: an emergency department, an area where time and clarity is important for optimal decision making and patient management.

In the emergency department, where an ECG is deemed to be necessary, the logical thought process for the reviewer is the following: Is this ECG normal or abnormal? If it is abnormal, is it an emergency? If it is abnormal but not an emergency, is it significant or non-significant?

We compared Cardiologs' solution to the widely used Veritas® conventional algorithm used on Mortara® ECG machines, following this logical thought process.

## Methods

This was a retrospective study of ECGs of patients presenting to the emergency department (ED) of Hennepin County Medical Center in Minneapolis (HCMC Minneapolis, MN, USA), a tertiary care hospital receiving approximately 100,000 emergency patients per year. Approval was obtained from HCMC institutional review board. The HIPAA Methods for De-identification of Protected Health Information were used.

All ED ECGs were recorded on Mortara machines, with the incorporated Veritas® automated interpretation immediately performed. Thus, the Veritas® algorithm was the only contemporary algorithm with which we could compare the DNN analysis system of Cardiologs®.

In order for this study to be representative of ECG application in an ED, we randomly selected ECGs recorded in the ED of HCMC. The electronic medical record (Epic) data management system at HCMC was searched for all ECGs recorded in the ED on patients aged 18 or older from July 1, 2015 to December 31, 2015. All HCMC ECGs used to train the DNN were from before this date; thus, none of the study ECGs had been used to train the DNN. From these ECGs, 1500 were randomly selected. The data includes the ECG signal in the raw digital format, the automated Veritas® algorithm ECG interpretation from the Mortara® Instruments ECG machines (Mortara, Milwaukee, WI), the physician confirmation ("overread") interpretation, and the department in which the ECG was recorded (Emergency Department, etc.).

The algorithm from Cardiologs predicts diagnostics from raw 12-lead ECG electrode recordings. It outputs the probability of presence of 76 different labels. These labels can correspond both to general classes of pathologies (e.g. ventricular rhythm) or to specific pathologies within these classes (e.g. ventricular tachycardia). Therefore, labels are non-exclusive, e.g. an ECG can be predicted to correspond both to ventricular rhythm and ventricular tachycardia. The final diagnostic consists in the list of labels with probability superior to 0.5. Importantly, we use a single model to predict the presence or absence of all labels simultaneously. This enables the model to take into account the dependence between pathologies. For example, when a patient has a preexcitation syndrome, the repolarization is affected by this preexcitation. The algorithm can then learn to disregard the ST elevation of a pseudoinfarction pattern in order to avoid the false alarm of STEMI.

The algorithm consists in a convolutional neural network with 16 layers, with the first 13 being convolutional layers, followed by 3 fully connected layers [15]. This is similar to VGG, a neural network used for computer vision [16]. The model was implemented in TensorFlow [17].

The model was trained using 100,000 ECG recordings for which the diagnostic was annotated by expert cardiologists. The training was done using stochastic gradient descent [15]. Briefly, at each training step, the model makes a prediction for an ECG, and this prediction is compared to the annotation from the expert cardiologist. Then, the parameters of the model are adjusted in order to lower the difference between predictions and annotations. This procedure is repeated for all ECGs in the training set, using each ECG multiple times. At testing time, the model is used to make predictions for each ECG in the testing set, and model predictions are compared against annotations. Importantly, the model was trained using data from multiple recording devices, and only a small portion of training examples were recorded using Mortara® ECG machine (5000 out of 80,000). Therefore, our algorithm is expected to be relatively device independent, and not limited to Mortara® ECG machine.

By comparison, the Veritas algorithm is embedded on the Mortara's ECG machine. Briefly, the Veritas algorithm consists in two steps: beats are first detected and compared to a representative beat generated using all artifact-free complexes from all 12 leads in the 10-s ECG recording [18]. Then, arrhythmia detection as well as QRS-T-U analysis is performed by extracting landmarks with proprietary methods. Such methods have not been publicly disclosed, except for QT/RR interval measurements [18–20].

Some previous studies have attempted to measure the performance of multi-label prediction in ECG diagnostics [21,22]. However, methodologies were restricted to a small number of possibly combined pathologies. For instance, studies of the accuracy of the Glasgow 12-lead ECG analysis program combined ventricular hypertrophy and myocardial infarction [21]. Willems et al. restricted experts' annotations to single labels [22]. Therefore, as stated above, no prior study has compared the performance of different algorithms in the global interpretation (both rhythm and QRS-T-U analysis) of unselected 12-lead ECGs, and so there was no precedent for methodology. Previous studies were limited to a small set of labels, including myocardial infarction and hypertrophies, but not to global ECG interpretation. But there are over 100

possible discrete labels (e.g., left bundle branch block, LBBB) that can be applied to any ECG, if present. Different algorithms do not have the same label (diagnosis) or set of labels for each ECG abnormality, and this complicates any comparison. Thus, it was necessary to create a new model for comparison. To do so, we prospectively mapped all labels for each algorithm to a standard set of groups.

It is not straightforward to define sensitivity and specificity in the case of multiple labels. Different alternatives exist, depending on how we define the "correctness" of a prediction. One could define a prediction to be correct if all pathologies and sub-pathologies are detected, and precisely detected. Using this definition, a prediction of "Bundle Branch Block" would be judged incorrect in the case of Left Bundle Branch Block because the prediction is not specific enough. However, as shown by this example, most predictions would be judged incorrect if they are not perfectly precise, even if they contain relevant information (here, "Bundle Branch Block" is more informative than "No Bundle Branch Block"). Alternatively, one could measure the correctness of predictions for each pathology individually. However, the specificity for infrequent labels such as "Left Bundle Branch Block," would be always close to 100%, even for a naive algorithm always predicting "No Left Bundle Branch Block."

In order to manage these obstacles, we prospectively agreed on a list of 17 groups of cardiac abnormalities able to express the whole range of possible interpretations at a less granular level than individual abnormalities (Table 1). This grouping made it possible to have a unified system for comparison of two different analysis systems. Furthermore, it helps to prevent ambiguities; for example, atrial fibrillation and flutter, which are often difficult for algorithms to differentiate, are grouped together (and then could be further classified into "significant" or "emergency" rhythms depending on a heart rate greater than, or less than, 120 bpm). STEMI and pericarditis, which are similarly difficult for algorithms to differentiate, are grouped together as acute emergencies. An automatic mapping from the two different annotation systems to this reduced list of groups was prospectively designed prior to the study initiation.

Furthermore, for the reasons outlined above, the statistical category of "true negative" for either individual labels or for the 17 groups was not applied; thus, we could not assess either specificity or negative predictive value. Analysis focused on the more meaningful categories of sensitivity and positive predictive value for identification of one or more of the 17 groups on each ECG.

We designed a comparison following the logical thought process of a reviewer in an emergency room where an ECG is deemed to be necessary. Is this ECG normal or abnormal? If it is abnormal, is it an emergency? If it is abnormal but not an emergency, is it significant or non-significant? Therefore, each of the 17 groups of conditions (16 abnormals, and 1 group for normal) (Table 1) was prospectively assigned an acuity category agreed upon by authors: "emergency" for abnormalities which require emergent treatment or consideration, "significant" for abnormalities that may have clinical significance to the emergency physician, but do not require immediate action, "non-significant" for abnormalities that are minor or non-specific, and "normal" for all normal or normal variant labels, including normal sinus rhythm and normal variant ST Elevation (also often called "early repolarization"). "Emergency" and "significant" abnormalities were together called "major" abnormalities.

Each ECG could have features of one or more groups. The final classification of each ECG into any category was made according to the most serious classification. For instance, if any group was in the emergency classification, even if others were not, then that ECG would be classified as "Emergency." For a more specific example: atrial fibrillation at a rate of 130/min with a left bundle branch block is classified as "emergency" because of the "rhythm emergency" (atrial fibrillation with rate ≥ 120), in spite of the fact that "bundle branch block" is only classified as "significant." Similarly, if the most severe feature was "significant", the final classification was significant even if all other features were "non-significant" or "normal."

**Table 1**
Definitions of the groups and categories.

| Category | Group | Description |
|---|---|---|
| Emergent | Rhythm emergency | Sinoatrial block/sinus paralysis, non-sinus supraventricular and pacemaker rhythms with HR < 45 or HR > 120/min |
| Emergent | Ventricular rhythm emergency | Ventricular rhythm (including short runs) with HR < 45 or HR > 120/min, indeterminate rhythms |
| Emergent | Atrioventricular (AV) conduction emergency | High-grade AV block: 2nd degree AV block Mobitz II or 3rd degree AV block |
| Emergent | Other acute emergency | Hyperkalemia, hypokalemia, acute ST Elevation MI, Acute Ischemia, recent MI, myocarditis/pericarditis |
| Emergent | Repolarization emergency | QTcF >500 ms (QTc, Fridericia: QTc = QT/√3(RR) (QT divided by cube root of RR interval) |
| Significant | Significant sinus rhythm | Sinus rhythm with HR < 45 or HR > 100/min |
| Significant | Significant rhythm | Non-sinus supraventricular and pacemaker rhythms with 45 < HR < 120/min |
| Significant | Significant ventricular rhythm | Ventricular rhythm (including short runs) with 45 < HR < 120/min |
| Significant | Significant AV conduction | Second degree AV block Mobitz I, Pre-excitation |
| Significant | Significant automatism | Supraventricular short runs, ventricular and atrial couplets/triplets/bigeminy/trigeminy |
| Significant | Significant bundle branch block | Complete right BBB, complete and incomplete left BBB, intraventricular conduction delay >130 ms |
| Significant | Ventricular hypertrophy | Ventricular hypertrophies |
| Significant | Old myocardial infarction | Old (previous) myocardial infarction, any location |
| Significant | Repolarization suggesting myocardial ischemia | Repolarization suggesting myocardial ischemia |
| Significant | Other significant abnormalities | Rare pathologies (pulmonary diseases, Brugada, dextrocardia, etc.), QTcF >470 and <500 ms, abnormal U wave, short QTcF (<320 ms) |
| Borderline | Non-significant | Isolated automatisms (premature atrial or ventricular beats), atrial hypertrophies, nonspecific abnormal QRS (left and right axes, fascicular blocks, IVCD >110 ms, incomplete RBBB), non-specific repolarization abnormalities, borderline QTcF (430-470 ms), first degree AV block, low voltage<br>This label is used on abnormal ECGs in absence of any other label (if a major label is present, this label is omitted) |
| Normal | Normal | Sinus rhythm with heart rate between 45/min and 100/min, including morphological normal variants (early repolarization etc.). |

*Abbreviations.* HR = heart rate. AV = atrio-ventricular. BBB = bundle branch block.

Since in acuity classifications (in contrast to the 16 abnormal groups) there was only one outcome for statistical analysis (major abnormality vs. none), acuity classifications could be assessed for true negatives and thus specificity and negative predictive value (NPV) could be calculated for this measure.

All ECGs were directly analyzed by the Veritas® algorithm at the time of ECG recording. The digital ECG signal was then fed to the Cardiologs® algorithm, which yielded an independent interpretation. For each ECG, the output report of each algorithm was mapped to the groups that had been chosen, as above.

The primary outcome was the performance of the algorithms in finding at least one "major" abnormality. The secondary outcome was the proportion of all ECGs for which all groups were identified, with no false negative or false positive groups ("accurate ECG interpretation"). Additionally, we measured sensitivity and positive predictive value (PPV) for any abnormal group. Finally, we also assessed the performance in identifying emergency groups.

*Reference standard*

Two experienced, blinded interpreters independently assessed each of 1500 ECGs. The interpreters chose all abnormalities identified on each ECG from a pick list, whether of rhythm, QRS, or ST-T-U waves. To this end, all ECGs were displayed on an ECG Analysis platform designed for this study, allowing the annotators to:

1) Visualize the ECG, with access to information such as the patient age, estimated delineation (the computerized onsets and offsets of waves), and standard measurements [heart rate, P-wave duration, P-wave axis, PR interval, QRS duration and axis, QT interval, and corrected QT (Fridericia)].
2) Manipulate the ECG in various ways, such as displaying the full 10 s of each lead when desired, decreasing the amplitude of the signals, measuring amplitudes and duration, and zooming in to observe fine details.
3) Provide a rhythm and QRS-T-U analysis interpretation.

Each interpreter was trained to use this ECG Analysis Platform by videoconference, and was given the ECG Analysis Platform Instructions for Use.

If, and only if, the initial expert interpretation resulted in a classification into discrepant "groups," (See Table 1 for the definitions of the 17 groups), the ECG was reviewed by a third ("tiebreaker") expert. If the tiebreaker disagreed with both interpretations, a consensus was reached with all interpreters participating. This final read was the reference standard, against which the automated interpretations were assessed. ECGs were excluded by interpreters if, in their opinion, the quality was inadequate or if there was lead misplacement. Importantly, none of these three interpreters had any access to Cardiologs' or Veritas' predicted diagnosis.

*Statistics*

The level of agreement comparing initial interpreters, and also comparing initial interpreters to the reference standard, was evaluated with percent agreement and kappa coefficient (with 95% CIs). Figures are given in proportions with 95% confidence intervals (CIs). Two-sided chi square tests were used to assess significance. McNemar's test was used to compare sensitivities.

Sample size was calculated based on analysis of 2.5 years of HCMC Emergency Department ECGs, in which the prevalence of major abnormalities (emergency findings plus significant findings) was 25%. Assuming a minimum value of 85% for either sensitivity or specificity, a sample of 1500 patients would give an acceptable 95% confidence interval of 81% to 88% for the sensitivity.

## Results

Of 24,123 ECGs recorded during the time period, 1500 ECGs were randomly selected; 27 were excluded because of artifact or lead misplacement, leaving 1473 ECGs. 559 interpretations (37.9%) resulted in discordant classification for one or more of the 17 groups and thus needed tiebreaking; hence, agreement on the full set of groups of initial interpreters was 62.1% (95CI 60.3–63.8). Among discrepant ECGs, 239 resulted in discrepant classification into normal vs. non-significant, and 7 required a consensus discussion. Out of 3191 initially annotated groups through the 2 interpretation rounds, 2124 were matches between both interpreters (66.6%, 95CI 64.9–68.2). Kappa between initial interpreters on acuity categories was 0.55 (moderate agreement). Agreement on acuity categories was 68.8% (66.4–71.2). Kappa between reference annotations and the initial interpreters was from 0.72 (substantial) to 0.81 (near perfect), and agreement ranged from 81% to 87%. Table 2 shows the count of abnormal groups.

**Table 2**
Count of abnormal groups.

| Group | Number | (%) |
|---|---|---|
| Rhythm emergency | 19 | 1.3 |
| Ventricular rhythm emergency | 2 | 0.1 |
| Other acute emergency | 33 | 2.2 |
| AV conduction emergency | 2 | 0.1 |
| Repolarization emergency | 4 | 0.3 |
| Significant sinus rhythm | 259 | 17.6 |
| Significant rhythm | 47 | 3.2 |
| Significant ventricular rhythm | 0 | 0.0 |
| Significant AV conduction | 3 | 0.2 |
| Significant automatism | 20 | 1.4 |
| Significant bundle branch block | 66 | 4.5 |
| Ventricular hypertrophy | 32 | 2.2 |
| Old myocardial infarction | 92 | 6.2 |
| Repolarization suggesting myocardial ischemia | 13 | 0.9 |
| Other significant abnormality | 18 | 1.2 |
| Nonsignificant | 402 | 27.3 |
| Normal | 574 | 39.0 |

AV = atrio-ventricular.
Note: because one ECG can have several groups of abnormalities, the figures of this table add up to >100%.

Fifty-two (3.5%) of 1473 ECGs had at least one emergent abnormality, for a total of 60 emergencies. There were 445 ECGs (30.2%) with 550 "significant" abnormalities. Thus, 497 ECGs (33.7%) had 610 "major abnormalities." There were 402 (27.3%) ECGs in the non-significant category, and 574 ECGs (39.0%) in the normal category. The largest of the 5 emergency groups was "other acute emergencies (STEMI, NSTEMI, pericarditis etc.)," with 33 of the total of 60 emergencies. Of the 445 ECGs with "significant" abnormalities, the most common by far was "significant sinus rhythm" due to sinus tachycardia ($n = 259$).

*Primary outcome: performance of classification of ecgs into major abnormality*

Table 3 shows the algorithm performance of acuity classification for major abnormalities. Accuracy was 77.6% (95% CI: 75.4–79.7) for Cardiologs® and 68.3% (95% CI: 65.9–70.6) for Veritas® ($p < 0.0001$). Because Cardiologs® had approximately half as many false positives, accuracy and especially specificity (94.0% vs. 84.7%) and PPV (88.2% vs. 75.4%) were significantly higher for Cardiologs®.

For acuity classification, Veritas® trended towards better sensitivity (92.0% vs. 88.7% ($p = 0.086$), with more true positives (457 vs. 441). However, in 9.2% (42/457) of those true positives, the group was incorrectly identified, compared with only 4.1% (18/441) for Cardiologs®. Thus, in approximately 9% of true positives for "major abnormality," vs. 4% for Cardiologs®, Veritas® made the correct classification of major abnormality through an incorrect diagnosis. This result is due to the fact that classifying an ECG as having an emergency abnormality did not necessarily imply that the found abnormality was correct: for instance, incorrectly finding ventricular tachycardia instead of STEMI would lead to a true positive. In fact, neither algorithm specifically identified the two ventricular rhythm emergencies, but both identified these ECGs overall as "emergency." Interestingly, both ECGs not only had initial discrepant interpretations but required consensus (See Table 5).

**Table 3**
Diagnostic performance of Cardiologs® vs. Veritas® for identifying an ECG with at least one major abnormality (emergency or significant) vs. none (non-significant or Normal).

| Major abnormalities | Cardiologs®, % (95% CI) | Veritas®, % (95% CI) | *p*-value |
|---|---|---|---|
| Sensitivity | 88.7 (85.7–91.2) | 92.0 (89.2–94.0) | 0.086 |
| Specificity | 94.0 (92.3–95.3) | 84.7 (82.3–86.9) | <0.0001 |
| PPV | 88.2 (85.1–90.7) | 75.4 (71.8–78.7) | <0.0001 |
| NPV | 94.2 (92.6–95.5) | 95.4 (93.8–96.6) | 0.27 |
| Accuracy | 92.2 (90.7–93.5) | 87.2 (85.4–88.8) | <0.0001 |

PPV: positive predictive value; NPV: negative predictive value.

**Table 4a**
ECGs with all groups correctly identified (no overcalls and no undercalls).

| | Cardiologs® | | Veritas® | | P |
|---|---|---|---|---|---|
| | Number | %, 95% CI | Number | %, 95% CI | |
| All ECGs | 1060/1473 | **72.0%** (69.6–74.2) | 881/1473 | **59.8%** (57.3–62.3) | < 0.0001 |
| ECGs with ≥1 abnormality | 567/899 | **63.1%** (59.9–66.2) | 517/899 | **57.5%** (54.3–60.7) | 0.016 |
| ECGs with ≥1 Major abnormality | 327/497 | **65.8%** (61.5–69.8) | 284/497 | **57.1%** (52.8–61.4) | 0.005 |
| ECGs with ≥1 Emergency | 24/52 | **46.2%** (33.3–59.5) | 23/52 | **44.2%** (31.6–57.7) | NS |

*Secondary outcome: correct identification of groups*

Table 4a shows groups correctly identified on all ECGs, on ECGs with ≥1 abnormality, ECGs with ≥1 major abnormality, and ≥1 emergency; Cardiologs® significantly outperformed Veritas® on all measures. Table 4b shows sensitivity for all abnormalities, for major abnormalities, and for emergencies; the algorithms were not significantly different. Finally, Table 4c shows PPV for all abnormalities, for major abnormalities, and for emergencies; because it had many fewer false positives, Cardiologs® significantly outperformed Veritas® in all categories.

We manually examined the false negatives at the label level, in detail (See Table 6a). The largest contingent of false negatives for both algorithms was clearly due to Non-STEMI. We similarly examined false positive emergencies (Table 6b). There were 15 false positive supraventricular rhythm emergencies for Veritas® vs. 5 for Cardiologs®. This reflects the difficulty for the Veritas® algorithm in differentiating between sinus tachycardia and other supraventricular rhythms. Additionally, Veritas®' measurements of QTc were often erroneous, and the algorithm overcalled STEMIs.

*Congruent vs. discrepant ECGs*

ECGs with initial discrepant interpretations (requiring tiebreaking) may be difficult and borderline ECGs; therefore, we compared the algorithms on the 914 congruent ECGs that had no discrepant groups (i.e., had concordant initial expert interpretations, and thus did *not* require tiebreaking). See Tables 7 and 8a-8c. For this group, the results mirror the larger cohort, except that in this group, in addition to having higher specificity and PPV, Cardiologs® also was more sensitive for abnormal ECGs and also for abnormal ECGs with at least 1 major abnormality.

**Table 4b**
Sensitivity for abnormal groups.

| | Cardiologs® | | Veritas® | | |
|---|---|---|---|---|---|
| | Number | %, 95% CI | Number | %, 95% CI | P |
| All abnormalities | 704/1012 | **69.6%** (66.7–72.3) | 691/1012 | **68.3%** (65.3–71.1) | NS |
| Major abnormalities | 464/610 | **76.1%** (72.5–79.3) | 458/610 | **75.1%** (71.5–78.4) | NS |
| Emergency abnormalities | 32/60 | **53.3%** (40.9–65.4) | 30/60 | **50%** (37.7–62.3) | NS |

**Table 4c**
Positive predictive value (true positives by the algorithm divided by all positives for that algorithm).

| | Cardiologs® | | Veritas® | | P |
|---|---|---|---|---|---|
| | Number | %, 95% CI | Number | %, 95% CI | |
| All abnormalities | 704/951 | 74.0% (71.1–76.7) | 691/1223 | 56.5% (53.7–59.3) | <0.0001 |
| Major abnormalities | 464/611 | 75.9% (72.4–79.2) | 458/812 | 56.4% (53.0–59.8) | <0.0001 |
| Emergency abnormalities | 32/52 | 61.5% (48.0–73.5) | 30/73 | 41.1% (30.5–52.6) | 0.024 |

## Discussion

Cardiologs has developed the first neural network able to detect multiple heart conditions simultaneously, using only the raw ECG signal as input. Here, we measured its performance for ECG applications representative of an emergency department. Compared to a reference standard, for classifying ED ECGs into major abnormality (emergency or significant), the Cardiologs®' DNN algorithm was significantly more accurate (92.2% vs. 87.2%), with significantly better specificity (94.0% vs. 84.7%) and PPV (88.2% vs. 75.4%) and a false discovery rate less than half of Veritas' (11.8% vs. 24.6%). Moreover, it was superior to the conventional algorithm in accurately identifying groups of abnormalities, with similar sensitivity (69.6% vs. 68.3%), and significantly better PPV (74.0% vs. 56.5%). Cardiologs identified the correct set of groups for 72.0% of ECGs, while Veritas identified only 59.8%.

For the subset of 914 ECGs that did not require tiebreaking, Cardiologs performed with higher sensitivity (84.1% vs. 78.8%), in addition to a higher PPV, for accurately identifying groups. Since Veritas is embedded in the Mortara machine, Veritas might be expected to perform better than Cardiologs; therefore, the better performance of Cardiologs, which is fully device-independent, is particularly noteworthy.

Over-diagnosis is recognized as a particular problem in computer-interpreted electrocardiograms [2,7]. Thus, although sensitivity for life threatening disorders is critical, specificity and PPV are also very important.

This study is the first to show the improved performance of a deep learning algorithm over a standard ECG interpretation algorithm on unselected 12-lead ECGs, although the improvement is modest. It may, in fact, be the first published direct comparison of automated ECG

**Table 5**
Manual investigation on the interpretation of the two ventricular emergency cases.

| | ECG1 | ECG2 |
|---|---|---|
| Cardiologs® | - Atrial flutter<br>- 2nd or 3rd degree AVB<br>- Complete right bundle branch block<br>- QTc > 500 ms | - Ischemia of indeterminate age<br>- Atrial fibrillation<br>- Ventricular pacemaker<br>- QTc > 500 ms |
| Veritas® | - Complete right bundle branch block<br>- Atrial tachycardia or flutter<br>- Ischemia of indeterminate age<br>- QTc > 470 ms | - Ventricular pacemaker<br>- Acute ischemia |
| Annotator 1 | - Atrial flutter<br>- Complete right bundle branch block | - Pacemaker<br>- Non-sustained ventricular tachycardia |
| Annotator 2 | - Atrial flutter<br>- Complete right bundle branch block<br>- QTc > 470 ms | - Ventricular pacemaker<br>- QTc > 500 ms |
| Reference (through consensus) | - Atrial flutter<br>- 3rd degree AV block<br>- Ventricular escape rhythm<br>- QTc > 470 ms | - Intraventricular conduction delay >130 ms<br>- Acute ischemia<br>- Ventricular pacemaker<br>- QTc > 500 ms<br>- Non-sustained ventricular tachycardia |

**Table 6a**
Manual investigation on the missed emergencies.

| | Total | Cardiologs® (missed) | Veritas® (missed) |
|---|---|---|---|
| Supraventricular rhythm >120 or < 45 | 19 | 1 | 0 |
| Ventricular rhythm >120 or < 45 | 2 | 0 | 0 |
| Complete heart block | 2 | 0 | 0 |
| Hyperkalemia | 2 | 0 | 1 |
| Hypokalemia | 1 | 1 | 1 |
| STEMI | 7 | 2 | 2 |
| Non STEMI | 20 | 16 | 13 |
| Recent or acute MI | 2 | 1 | 1 |
| Myocarditis/pericarditis | 1 | 0 | 0 |
| QTcF > 500 ms | 4 | 1 | 3 |
| Total | 60 | 22 | 21 |

algorithms [2]. Interesting questions arise from this study, in particular concerning what is the ECG reference standard for some structural abnormalities (QRS-T-U), and what would be the performance of actual physicians, either overreading the algorithm or not, compared to the algorithms.

ECGs are interpreted in the clinical context by non-experts in real time with the aid of the automated interpretation. We know that the final ECG interpretation is greatly influenced by the automated interpretation, and sometimes in error, with clinical consequences [1,5–8]. An ideal study, in the clinical context, would be to randomize the automated interpretation to the DNN vs. contemporary algorithm. We could then use the final clinical physician over-read for comparison to an expert reference standard, or even to outcomes and patient management, to assess carefully ruling in one possibility and ruling out the other, based on clinical and laboratory data.

Previous neural networks for ECG interpretation had many limitations. Most neural networks, though they can also learn on their own, are trained to find ECG abnormalities based on input of a simplified representation of an ECG, with handcrafted features such as the ST elevation value [23,24]. Others have a single simplified output such as acute MI [23,24], or AV block [25]. Others have a list of exclusive outputs defining an ECG or a beat [such as left bundle branch block (LBBB) vs. right BBB (RBBB) vs. paced vs. ventricular vs. normal vs. other] [26–28]. Others analyze rhythm only, and one exceeded the performance of board certified cardiologists for this task [12].

Cardiologs®' algorithm is the first deep neural network algorithm that uses directly the whole 12-lead ECG as input, without any instructions, and interprets the whole 12-lead ECG. One additional reason for its success is that this neural network, unlike the conventional algorithms, has "non-exclusive" labels: this means that the single neural network algorithm can produce several labels (one for each abnormality) on a unique ECG, whereas the conventional algorithms use a separate sub-algorithm for each abnormality or set of disjointed abnormalities. For instance, if an ECG has both "atrial fibrillation" and "left bundle branch block," the quality of the interpretation is improved since the detection of a left bundle branch block can then help the algorithm to differentiate sinus rhythm from a ventricular rhythm. The conventional approach is to have two separate instructions (two different algorithms) for these two different outputs and to produce independent labels that are unrelated. In such a conventional algorithm, one label does not contribute to the diagnosis of another label, although simple rules can deactivate labels when the combination does not make sense (e.g., bundle branch blocks in case of ventricular tachycardia). It may diagnose both atrial fibrillation and left bundle branch block, but the diagnosis of either one does not affect the diagnosis of the other.

**Table 6b**
Manual investigation on the false positives of emergencies.

| | Cardiologs® | Veritas® |
|---|---|---|
| Supraventricular rhythm <45 or > 120 | 5 | 15 |
| 2nd degree AV Block, Mobitz II | 0 | 1 |
| Hyperkalemia | 1 | 1 |
| STEMI | 0 | 8 |
| Non-STEMI | 0 | 1 |
| Recent MI | 2 | 0 |
| Pericarditis or myocarditis | 5 | 5 |
| QTc > 500 ms | 5 | 11 |
| Total | 18 | 42 |

**Table 7**
Diagnostic Performance of Cardiologs® vs. Veritas® for identifying an ECG with at least one major abnormality, among the 914 cases that did not require tiebreaking.

| Major Abnormalities | Cardiologs®, % (95% CI) | Veritas®, % (95% CI) | p-value |
|---|---|---|---|
| Sensitivity | 98.0 (95.6–99.1) | 96.6 (93.8–98.1) | 0.22 |
| Specificity | 96.6 (94.9–97.8) | 88.6 (85.8–90.8) | <0.0001 |
| PPV | 93.2 (89.8–95.5) | 79.9 (75.5–83.8) | <0.0001 |
| NPV | 99.0 (97.9–99.5) | 98.2 (96.7–99.0) | 0.24 |
| Accuracy | 97.0 (95.7–98.0) | 91.1 (89.1–92.8) | <0.0001 |

PPV: positive predictive value; NPV: negative predictive value.

The neural network directly produces 75 "non-exclusive" labels (other labels are added afterwards based on measurements such as heart rate and QT intervals). Because of these non-exclusive labels, it can also produce outputs of different granularity. For ECGs with a high degree of difficulty, it was designed to produce a more general (less granular) interpretation. For instance, it may give the less precise interpretation of "atrial fibrillation or flutter" in a case of atrial fibrillation that is difficult to differentiate from atrial flutter. Handling these different levels of granularity was done using an ontology of cardiovascular diseases. Similar methods yielded positive results in other fields such as dermatology [10].

Neural networks need a training phase in order to tune their numerous parameters so that it outputs an accurate interpretation when an ECG is provided as input. The interpretation is expressed as a sequence of values representing the probability of presence of each abnormality in the whole ECG. For instance, if a premature atrial complex (PAC) is present anywhere in the ECG, the sequence will contain a "1" at the index corresponding to the "PAC" label. Only the presence or absence of the abnormalities is given to the algorithm; no information is given on the location of the abnormality, or on the reason that it was interpreted as such. During each step of training, an ECG is provided to the neural network, which outputs an interpretation. This interpretation is then compared to the expected interpretation. The parameters of the neural network are slightly modified so that the interpretation gets closer to the expected interpretation. For this first version, this process was repeated countless times with approximately 130,000 ECGs and their corresponding interpretations. ECGs have been and will be continually added in the future to further refine the algorithm, so that it is always improving. As of the end of 2017, the DNN has been trained on approximately 170,000 ECGs.

### *Limitations*

The most important limitation was that the two algorithms do not have exactly identical individual labels. Thus, the labels from each had to be mapped to the 17 groups. Furthermore, many groups were represented by small numbers, including the absence of any ventricular rhythms and only 3 AV conduction disturbances. Emergencies had particularly low numbers (total, 60), which made it difficult to meaningfully compare and contrast the sensitivities of the algorithms for emergencies, even with such a large dataset. This limitation is the direct result of the main strength of the study: it represents a random sample of real-life ED ECGs rather than a selection of highly abnormal ECGs. Moreover, the large number of normal and non-significant ECGs made for a powerful comparison of specificity and PPV. Some groups of emergencies were heterogeneous, such as grouping STEMI with Pericarditis; since these may be difficult to differentiate for both clinicians and

**Table 8a**
ECGs with all Groups correctly identified (no overcalls and no undercalls)
Comparison of algorithms in Cases in which the initial expert interpretations were congruent (did not need tie-breaking). $N = 914/1473$ total (62.1%).

| | Cardiologs® | | Veritas® | | P |
|---|---|---|---|---|---|
| | Number | %, 95% CI | Number | %, 95% CI | |
| All ECGs | 779/914 | 85.2% (82.8–87.4) | 645/914 | 70.6% (67.5–73.4) | <0.0001 |
| ECGs with ≥1 abnormality | 400/504 | 79.4% (75.6–82.7) | 353/504 | 70.0% (65.9–73.9) | 0.0007 |
| ECGs with ≥1 Major abnormality | 249/293 | 85.0% (80.4–88.6) | 216/293 | 73.7% (68.4–78.4) | 0.0008 |
| ECGs with ≥1 Emergency | 17/21 | 81.0% (60.0–92.3) | 15/21 | 71.4% (50.0–86.2) | 0.4687 |

algorithms, we grouped them primarily to assess the algorithms' recognition of an emergency, with the rationale that once warned of the presence of emergency, the clinician would be prompted to assess carefully.

Since the experts used Cardiologs®' platform for the annotations, they may have also been biased by the measurements (of QT interval, or QRS duration, or heart rate) that were provided to them. Indeed, these measurements are the ones used by the algorithm for measurement-based abnormalities such as the PR interval. Experts were however also provided with tools for checking the measurements themselves in order to thwart this bias, which is limited to only a few labels. More importantly, very few major abnormalities or accurate interpretations were dependent on these measurements.

Another limitation was the reference standard, which depended on expert interpretation. This limitation is particularly acute for Non-STEMI. We did not have anatomic or physiologic outcomes data for each ECG. However, in clinical practice, ECGs are interpreted by machines with human oversight. In future studies, the reference standard should perhaps always be consensus of the experts.

Because all ECGs in the training and testing set were recorded before July 1, 2015, and all used for this study were from after that date, no ECG that was used for training could have been used in the study. However, because of the need for ECG de-identification for patient privacy, we could not be certain that a patient whose ECG was in the study did not have a different previous ECG recorded that had been used for training. However, this is of little consequence for two reasons. First, there would have been little overlap because the testing set is composed of 1500 ECGs, which were sampled randomly among 30,000 ECGs, and the training set was composed of 5000 ECGs from Mortara's device, which were selected out of 80,000 possible ECGs. Second, ECGs from one individual are not perfectly constant over time; they change with changing patient condition, and would be unlikely to be substantially similar.

Finally, it would be interesting to compare the performance of Cardiologs' solution of ECG analysis in the ED to other existing algorithms. However, this was hindered by multiple factors. First, other solutions are either embedded on recording devices (e.g., GE Marquette™ 12SL or Philips DXL) or proprietary (like Glasgow® by Physio-Control) [21]. In both cases, we did not have access to these algorithms' predictions for our ECGs from an ED. Second, we could have used performance statistics reported in other previous studies. However, contrary to standard belief, sensitivity and specificity do differ in populations with widely differing prevalence of pathologies [29]. Here, in order to make this study as meaningful as possible in the context of emergency medicine, we studied a population representative of patients presenting to an ED, in which the prevalence of each entity is very low. In previous studies, the prevalence of each studied entity was either very high, or only one element (e.g., acute myocardial infarction) was studied [21,23,30,31]. Therefore, we expect to measure different performances than those reported in studies with different populations. Historical controls (i.e., performance characteristics from other studies) are furthermore not appropriate because no two ECGs are the same, which would render comparison inaccurate. Third, we propose a unique algorithm making predictions for all of multiple pathologies simultaneously. However, aside from Veritas, other methods omit many or even most pathologies that are predicted by Cardiologs' solution, which again makes comparison impossible [32–40]. While some pathologies like atrial fibrillation are often addressed [32–34], some other pathologies such as idioventricular rhythm or pericarditis are rarely addressed. Therefore, most proposed methods are not suitable for comparison with Cardiologs' algorithm concerning simultaneous detection of multiple pathologies.

## Conclusion

The Cardiologs®' ECG algorithm, the first deep neural network automated 12-lead ECG interpretation algorithm, performed significantly better than Veritas®' algorithm, identifying ECGs with major abnormalities with a higher positive predictive value while maintaining equal sensitivity. It had a significantly higher rate of accurate ECG interpretation, with similar sensitivity and higher PPV.

## Funding

All funding was by Cardiologs® Technologies.

The first author, Dr. Stephen W. Smith, received no funding and received no financial support of any kind from any source.

## Disclosures

Brooks Walsh – paid by Cardiologs® a set fee for blind interpretation of ECGs.

Kyuhyun Wang – paid by Cardiologs® a set fee for blind interpretation of ECGs.

Ken Grauer – paid by Cardiologs® a set fee for blind interpretation of ECGs.

Jia Li – employed by Cardiologs®, shareholder in Cardiologs®.

**Table 8b**
Sensitivity for abnormal groups.

| | Cardiologs® | | Veritas® | | P |
|---|---|---|---|---|---|
| | Number | %, 95% CI | Number | %, 95% CI | |
| All abnormalities | 448/533 | 84.1% (80.7–86.9) | 420/533 | 78.8% (75.1–82.1) | 0.0001 |
| Major abnormalities | 297/322 | 92.2% (88.8–94.7) | 283/322 | 87.9% (83.9–91.0) | 0.0043 |
| Emergency abnormalities | 20/23 | 87.0% (67.9–95.5) | 17/23 | 73.9% (53.5–87.5) | 0.375 |

**Table 8c**
Positive predictive value (true positives by the algorithm divided by all positives for that algorithm).

| | Cardiologs® | | Veritas® | | P |
|---|---|---|---|---|---|
| | Number | %, 95% CI | Number | %, 95% CI | |
| All abnormalities | 448/527 | 85.0% (81.7–87.8) | 420/671 | 62.6% (58.9–66.2) | < 0.0001 |
| Major abnormalities | 297/347 | 85.6% (81.5–88.9) | 283/439 | 64.5% (59.9–68.8) | < 0.0001 |
| Emergency abnormalities | 20/28 | 71.4% (52.9–84.7) | 17/33 | 51.5% (35.2–67.5) | 0.1126 |

Jeremy Rapin – employed by Cardiologs®, shareholder in Cardiologs®.

William Fennell – no disclosures.

Pierre Taboulet – shareholder in Cardiologs®.

Stephen Smith – no disclosures.

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