

# Clinical Validation of the New 12-lead ECG-based Noninvasive Beat-to-Beat Panoramic Epi-endocardial Mapping Technology

Mikhail Chmelevsky<sup>1,2,3</sup>, Stepan Zubarev<sup>1,3</sup>, Svyatoslav Khamzin<sup>1</sup>, Arsenii Dokuchaev<sup>1</sup>, Anastasia Bazhutina<sup>1</sup>, Margarita Budanova<sup>1,3</sup>, Aleksandr Sinitca<sup>1</sup>, Dmitry Lebedev<sup>3</sup>, Angelo Auricchio<sup>2</sup>

<sup>1</sup>XSpline S.p.a., Bolzano, Italy

<sup>2</sup>Fondazione Cardiocentro Ticino, Lugano, Switzerland

<sup>3</sup>Almazov National Medical Research Centre, Saint-Petersburg, Russia

## Abstract

This study introduces a novel noninvasive panoramic epi-endocardial mapping technology utilizing a 12-lead ECG, designed to overcome the limitations of traditional electrocardiographic imaging systems that require 150-250 ECG body surface recordings. The technology was tested on twelve heart failure patients with typical and atypical Left Bundle Branch Block (LBBB), incorporating machine learning algorithms for enhanced accuracy. Comparisons with biventricular endocardial electroanatomic contact mapping (EAM) showed that the system accurately identified all early and late activation

patterns. The correlation of the endocardial noninvasive activation maps with EAM data was high, with an average of 0.92, and a mean absolute error between 9-15mm, demonstrating high precision of novel technology. This innovative approach shows significant promise for accurate reconstruction of endocardial electrical activation maps. The study findings suggest this technology could substantially enhance diagnostic accuracy and treatment efficacy while it's potential for clinical application is particularly relevant in pre-procedural planning for device implantation and catheter ablation.

### Anatomical Assessment

Automatic AI based segmentation tool for ventricles and coronary sinus veins

### Electrical Assessment

Precise Non-Invasive Epi-Endocardial Electro-Anatomical Map Based on a Standard 12-Lead ECG

### Target zone identification

Target zone identification for successful LV electrode implantation

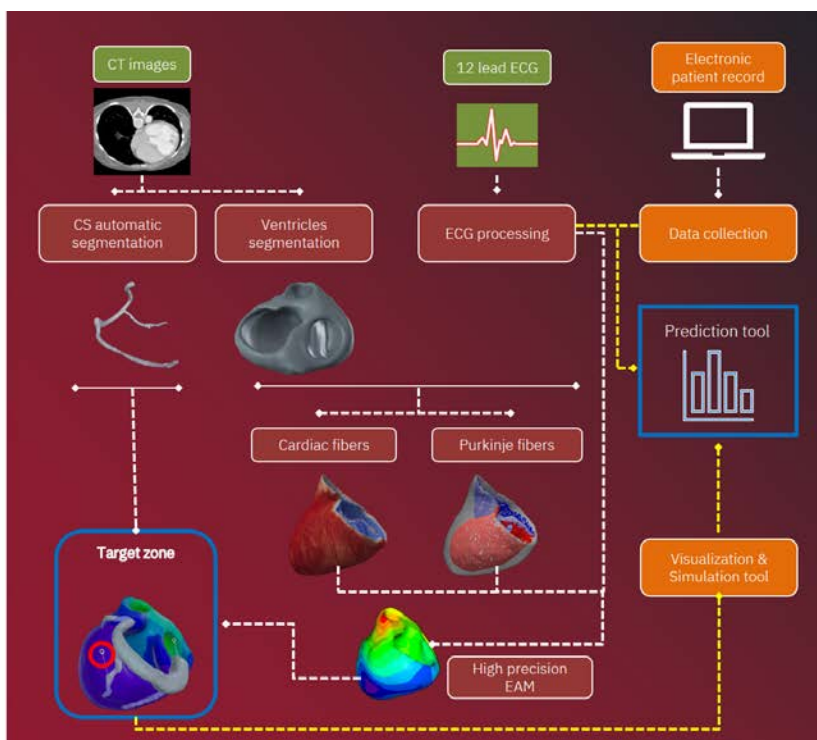
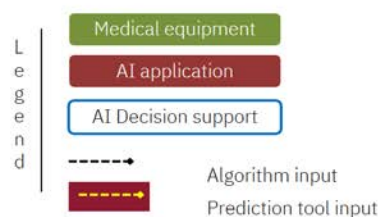


Figure 1. Overview and General Scheme of the Novel 12-Lead ECG Noninvasive Panoramic Epi-Endocardial Mapping

## 1. Introduction

Noninvasive electrocardiographic imaging (ECGI) presents a significant advancement in cardiac diagnostics, transcending the limitations of standard ECG by integrating data from numerous electrodes (typically between 150 to 250) with detailed anatomical information of the heart and torso. This integration allows ECGI to map cardiac electrical activity with far greater detail and accuracy. Such capabilities are particularly valuable in diagnosing and guiding treatment for complex arrhythmias. ECGI also plays a pivotal role in Cardiac Resynchronization Therapy (CRT) by providing detailed maps of heart electrical activity and latest activation zones, which are crucial for optimizing LV lead placement and enhancing therapy effectiveness [1].

Despite its proven efficacy in various studies, the practical application of ECG mapping in clinical settings is impeded by its requirement for numerous structures, the necessity for manual segmentation of cardiac imaging during CT/MR imaging acquisition, and the need for specialized technical support, all contributing to increased costs.

Moreover, conventional noninvasive mapping systems are generally limited to depicting only epicardial activation, omitting crucial endocardial details. To bridge this gap and also address other limitations recent innovations have employed machine learning (ML) algorithms to refine the precision of ECG forward-inverse calculations. A breakthrough in this field is a novel fully automated system for noninvasive panoramic epi-endocardial mapping that operates solely on a standard 12-lead ECG. This technology leverages cutting-edge ECGI techniques and deep ML integration for the automatic segmentation of cardiac structures and rapid generation of noninvasive electrical activation maps (Figure 1).

The potential of this technology is immense, but its clinical efficacy and accuracy must be meticulously validated with real clinical data to ascertain its suitability and value in everyday clinical practice.

## 2. The aim of the study

The objective of this study was to perform clinical validation of a novel technology that generates electrical activation maps based solely on 12-lead ECG data, comparing them directly with standard invasive contact mapping systems. The goal was to demonstrate the accuracy with which the noninvasive technology can reconstruct electrical activation maps and to evaluate the average error in these reconstructions.

## 3. Materials and methods

### 3.1. Patients and clinical data

Twelve heart failure patients (7 males, median age: 65) with QRS duration (min–max) 146–224 ms underwent cardiac CT scans and 12-lead ECG recordings. The ECG showed typical left bundle branch block (LBBB) in 7 cases and atypical LBBB in the rest.

Subsequently, patients were scheduled for conventional CRT implantation. Prior to operation procedure, a bi-ventricular endocardial electroanatomical contact mapping (EAM) using the Carto system (Biosense Webster, Inc., US) was performed for the left and right ventricles (LV and RV, respectively). A median of 258 (range 181-576) local electrograms in the LV and 86 (range 70-139) in the RV were collected during EAM. Written informed consent was obtained from each patient before the procedures. The study received approval from the local institutional review board.

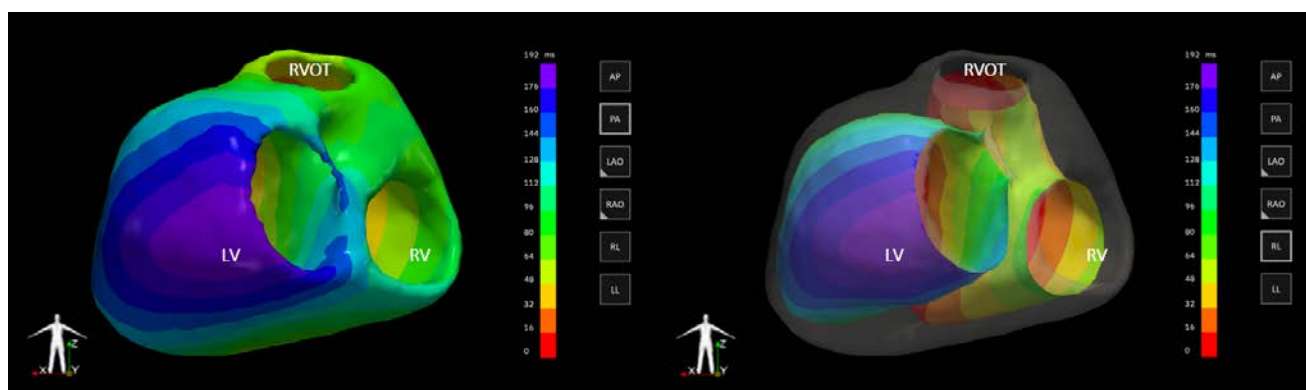


Figure 2. Visualization of 3D Noninvasive Electrical Activation Maps Derived from 12-Lead ECG using XSpline System in Postero-Anterior (PA) Projection. LV – Left Ventricle, RV – Right Ventricle, RVOT – Right Ventricle Outflow Tract. The left side of the figure displays the comprehensive epi-endocardial activation map, while the right side illustrates the endocardial activation map, featuring a semi-transparent epicardial surface for enhanced depth perception and detail.

### 3.2. Data Processing and Model comparison

All data from the invasive Carto mapping system was extracted in digital format and uploaded into custom-written software using Python (Python Software Foundation). This data included the position of mapping points with x, y, z coordinates, local activation times at each point, and endocardial anatomical structures represented as a mesh 3D object.

Noninvasive epi-endocardial activation maps were generated using advanced mathematical models, including machine learning methods, and automatically segmented cardiac CT data in the XSpline software (XSpline S.p.A., Italy). The results are presented in Figure 2. This data was also extracted as digital files representing 3D meshes of the ventricles with activation times at each point.

Subsequently, the two mesh models from the invasive Carto system and noninvasive XSpline data were imported into custom software and fused using the iterative closest point algorithm. This algorithm computes an optimal affine-based registration for the fusion of two surfaces. Both quantitative and qualitative comparisons were performed post-fusion. The registration error was calculated as the mean distance from each vertex on the Carto system 3D mesh model to the nearest vertex on the registered XSpline 3D mesh model. A map of absolute distances between the fused models was created for further analysis.

### 3.2. Statistical analysis and validation metrics

Several metrics were used to validate the noninvasive mapping against the invasive EAM. Spearman correlation ( $r$ ), mean absolute error (MAE), and relative distance

metrics were used to quantify the distance between the two late activation points determined invasively and non-invasively. Additionally, a novel metric was introduced to evaluate the spatial accuracy of noninvasive mapping in reproducing the detailed ventricular activation sequence. This involved analyzing the dispersion and alignment of activation patterns across various cardiac segments. The comparative analysis was further enhanced by examining the degree of congruence in identifying areas of delayed activation or scar tissue, crucial for CRT efficacy.

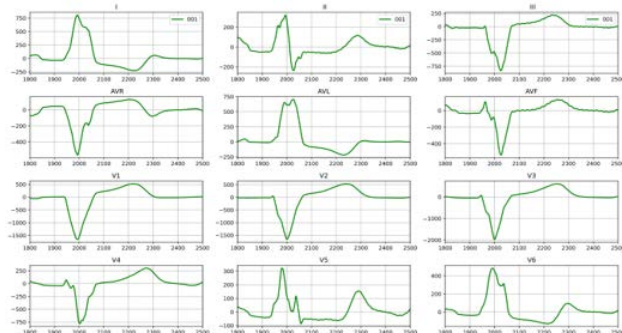


Figure 3. An example of 12-Lead ECG from a Patient with Typical LBBB utilized for the calculation of the noninvasive activation map with the XSpline system

## 4. Results

### 4.1. Qualitative Analysis of the Electrical Activation Maps

The qualitative analysis involved a comprehensive review of all cases by three highly experienced cardiac electrophysiologists. The novel 3D panoramic noninvasive mapping technology accurately captured early and late

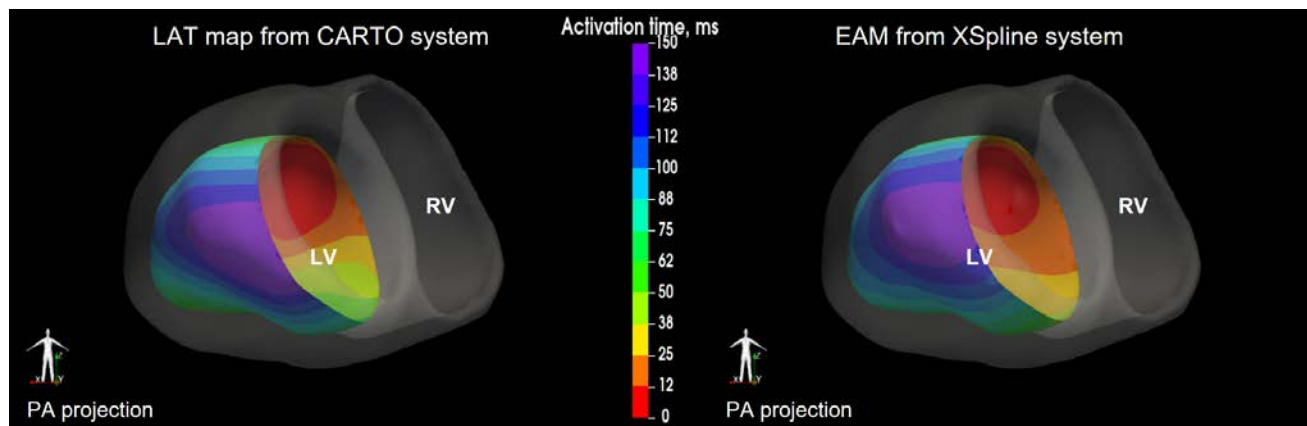


Figure 4: Comparative Visualization of Endocardial Electrical Activation Maps in a Patient with Typical LBBB. The left side of the image shows the activation map generated from the Carto system, while the right side depicts the corresponding map derived from the XSpline System, utilizing data from a standard 12-Lead ECG in Postero-Anterior (PA) Projection

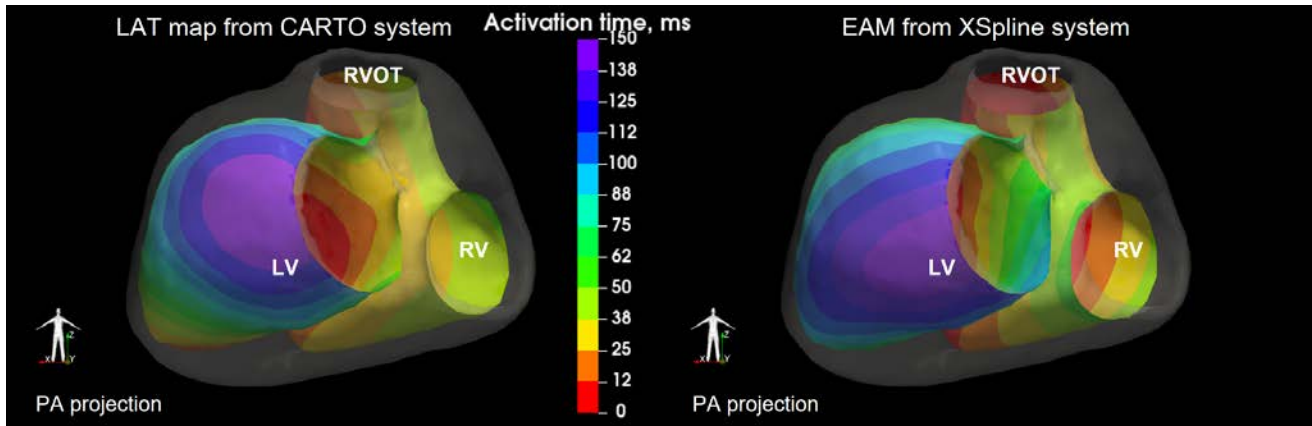


Figure 5: Comparative Visualization of Endocardial Electrical Activation Maps in a Patient with Atypical LBBB. The left side of the image shows the activation map generated from the Carto system, while the right side depicts the corresponding map derived from the XSpline System, utilizing data from a standard 12-Lead ECG in Postero-Anterior (PA) Projection

activation patterns on both epicardial and endocardial surfaces. While the electrical activation maps were not identical in every detail, the main activation patterns were consistently similar across all cases. This analysis was divided into two groups: those with typical Left Bundle Branch Block (LBBB) and those with atypical LBBB. In the typical LBBB group, the location of the latest activation zone was consistently identified in the anterolateral or inferolateral basal segment of the left ventricle. An example of this comparison, including the corresponding ECG, is presented in Figure 3 and Figure 4, respectively. For patients with atypical LBBB, the latest activation zone's location varied slightly, but the overall activation pattern remained uniform. An example of this can be seen in Figure 5, with the corresponding ECG in Figure 6.

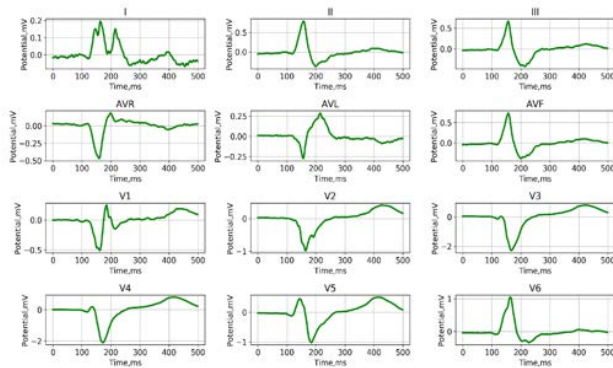


Figure 6. An example of 12-Lead ECG from a Patient with Typical LBBB utilized for the calculation of the noninvasive activation map with the XSpline system

## 4.2. Qualitative Analysis

Quantitative analysis of the endocardial activation maps

revealed an average correlation of 0.92 for cases with typical LBBB, demonstrating high concordance with the clinical ECGs ( $r = 0.96$ ). A correlation coefficient of 0.89 was obtained when comparing noninvasive and invasive ECGs. The average distance error between the non-invasive late activation zone and the CARTO data was 14 mm, with a MAE ranging between 9-15 mm. For cases with atypical LBBB, similar metrics were observed: Mean correlation:  $r = 0.87$ , and Mean late activation zone (LAZ) distance error: 16 mm

## 5. Discussion and Conclusions

This study validates the effectiveness of a novel mapping technique that leverages 12-lead ECG and cardiac CT scans to reconstruct endocardial electrical activation maps. The findings underscore that this new noninvasive mapping technology is ready for clinical implementation.

The introduction of this innovative technology marks a significant step forward in the realm of cardiac diagnostics and treatment. It enables the precise calculation of electrical maps noninvasively, and further integration of this technology into routine clinical practice holds the promise of transforming the approach to cardiac care, making it more efficient, less invasive, and more accurate.

## References

- [1] S. Pezzuto *et al.*, "Reconstruction of three-dimensional biventricular activation based on the 12-lead electrocardiogram via patient-specific modelling," *Europace*, vol. 23, no. 4, pp. 640–647, 2021, doi: 10.1093/europace/euaa330.

Address for correspondence:

Dr. Mikhail Chmelevsky  
e-mail: electrocardiologylab@gmail.com