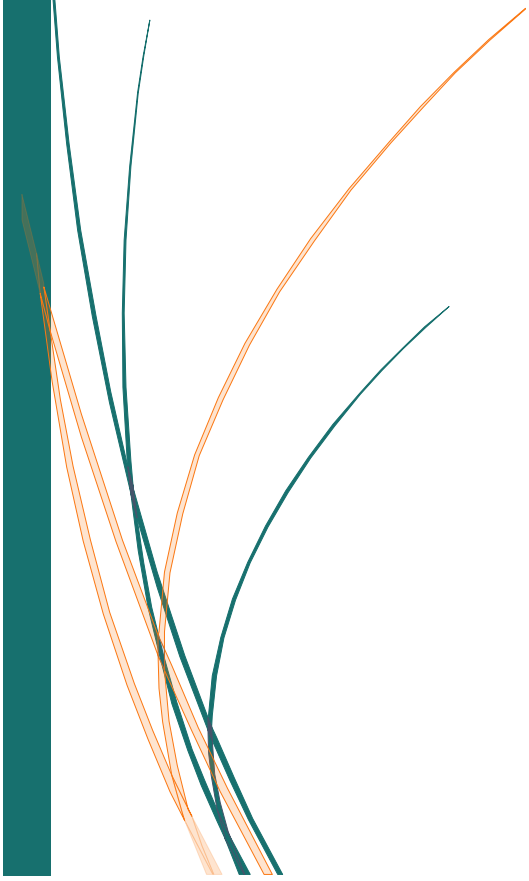
2022

R&D Portfolio

ECG Excellence



ECG-Excellence

Contents

Model Basis

Establishment of Modeling Methodology

Paper 1

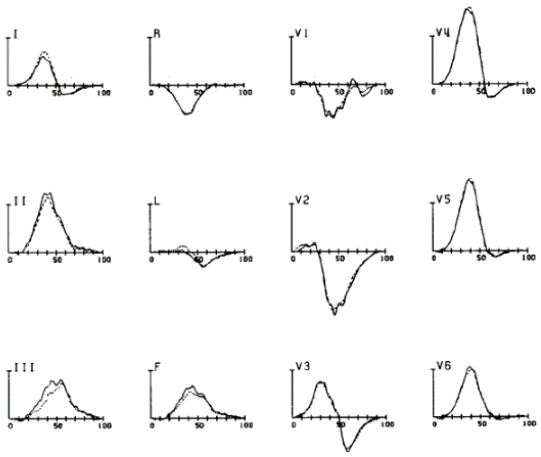
Lead author:	Huiskamp, GJ	**Year:**	1988
Institution/s:	Radboud University Nijmegen		
Journal:	IEEE Transactions on Biomedical Engineering		
Reference:	*Huiskamp G & Van Oosterom A. The depolarization sequence of the human heart surface computed from measured body surface potentials. IEEE Trans Biomed Eng. 1988;35:1047-58.*		

Contribution to ECG Excellence technology:	First time the depolarization sequence could be estimated from a healthy subject with the equivalent dipole source model

Abstract:

A method for computing the activation sequence at the ventricular surface from body surface potentials, validated previously in a model-to-model study, has been adapted to handle measured data. By using measured anatomical data together with a 64-channel ECG recording of the same subject for three subjects, it is shown that the model is able to determine activation sequences on the heart surface which closely resemble similar such data obtained through invasive measurement as reported in literature.

The inverse problem in electrocardiology deals with the clinically relevant question of determining cardiac electrical sources from potential measurements on the torso surface. Any solution method always requires an adequate source model description, together with a solution method for the implied forward problem, which is a problem of volume conduction. In our study, both the basic source model and the forward solution method used are well-known. The specific variant of the dipole-layer model used has some very attractive properties regarding the solution of the associated inverse problem. Recent work on this variant has shown that stable inverse solutions can be obtained in a model-to-model approach. The availability of full-body surface potential data and an accurate description of the volume-conductor geometry of a number of healthy subjects together with further conceptual simplification and some ''streamlined' ' computer programming has led to the possibility of applying the acquired method to measured data. This results in maps of isochrones of activation of the actual surface of the heart, deduced from measured potentials and actual geometry data of that same subject.



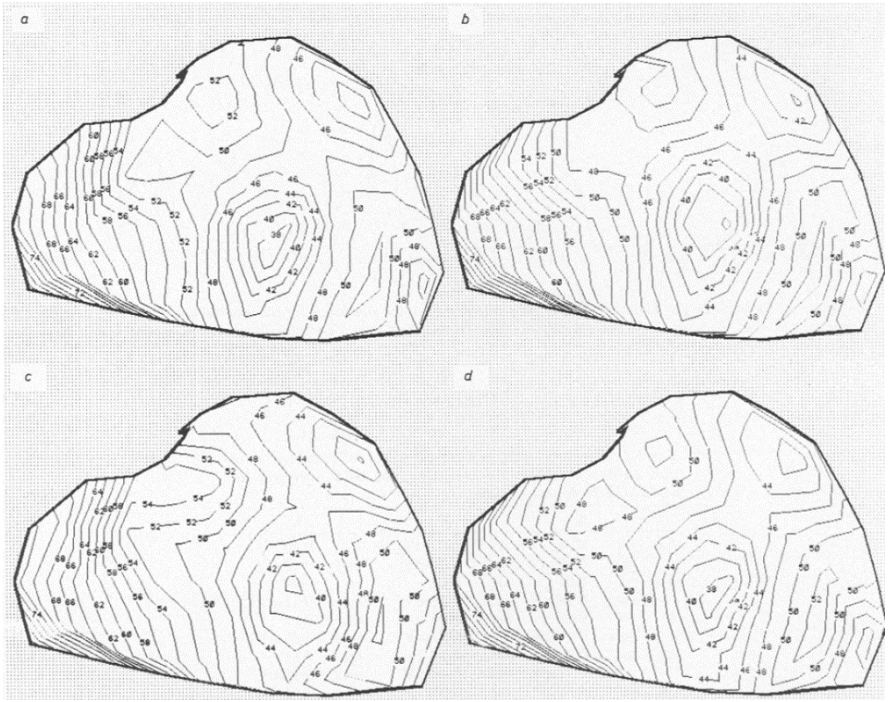
Paper 2

Lead author:	Huiskamp, GJ	Year:	1992
Institution/s:	Radboud University Nijmegen		
Journal:	Medical & Biological Engineering & Computing		
Reference:	*Huiskamp GJ & van Oosterom A. Heart position and orientation in forward and inverse electrocardiography. Med Biol Eng Comput. 1992;30:613-20.*		

Contribution to ECG Excellence technology:	Investigated the influence of the heart geometry variations on the used forward and inverse procedure.

Abstract:

A study has been made of the influence of the orientation and position of the heart within the thorax on computed ECG signals (forward modeling) in three normal subjects. Results show that differences in heart position and orientation, associated with shifts relative to of about 5 mm can result in ECG amplitude differences in the order of tenths of mV, also found in the interindividual differences in the ECG signals. The inverse modeling results show that, despite these differences the solutions were stable for the ventricular activations sequence. However for subjects where the precordial leads were very close to the heart surface the inverse solution was found to be intrinsically poor.



Paper 3

Lead author:	van Oosterom, A	Year:	2001
Institution/s:	Radboud University Nijmegen		
Journal:	Journal of Electrocardiography		
Reference:	*van Oosterom A. Genesis of the T wave as based on an equivalent surface source model. Journal of Electrocardiography. 2001;34:217-227.*		

Contribution to ECG Excellence technology:	Provides the mathematical background for using the equivalent dipole layer, as used in the ECG Excellence technology, both for depolarization and repolarization

Abstract:

Background: This article shows the use of the equivalent surface source model in its application to the genesis of the surface ECG in which the sources are of the double layer type. This model has previously been shown to yield an accurate description of body surface potentials during the QRS interval. Its application to the genesis of the T wave is now worked out in greater detail.

Methods and Results: In this source model, the full spatio-temporal character of the cardiac electric generator is expresses by means of an equivalent double layer situated at the boundary of ventricular tissue. The timing of local depolarization and of repolarization of the cells near this boundary is used to simulate the surface ECG. The background of this source model is discussed, as well as its validity. A matrix formulation is presented of the forward problem of computing the resulting body surface potentials. Based on this forward formulation, an inverse computation of the timing of the repolarization process was performed. Simulated T waves, based on this timing, showed a close correspondence with measured body surface potentials.

Conclusions: By taking the inversely computed timing of repolarization as representing the true situation, the model can be used to study in which way perturbations in the timing of local repolarization effect the shape of the T waves. An analysis based on this model indicates that the amplitude of the T wave is proportional to the dispersion of the repolarization times at the ventricular surface. The model is also shown to be capable of simulating the ECG changes during local ischemia.

$$\varphi(\vec{y}) = -\int_{S_h} g_i \varphi_m(\vec{x}) \nabla Z \cdot d\vec{S}_h, \tag{2}$$

(his Eqn. 68), now involving an integration over the surface S_h and $\vec{x}$ specifying the source location on S_h. For potentials φ_∞ in an hypothetical, infinite homogenous medium surrounding the heart, Z can be shown to be

$$Z(\vec{y},\vec{x}) = \frac{1}{4\pi\sigma_o R}, \tag{3}$$

with σ_0 the conductivity of the medium and R the distance between $\vec{x}$ and $\vec{y}$ (see, *e.g.*, [9]). Substitution of Eqn. 3 in Eqn. 2 leads to

$$\varphi_\infty(\vec{y},t) = -\frac{g_i}{4\pi\sigma_0}\int_{S_h} \varphi_m(\vec{x},t)\nabla\frac{1}{R}\cdot d\vec{S}_h. \tag{4}$$

This expression is valid at all time instants t. In deriving this result Geselowitz used the boundary condition $g_i \nabla\varphi_m \cdot d\vec{S}_h = 0$, a boundary condition also used in the work of Colli-Franzone *et al.*[10] (see also the discussion on this boundary condition in Chapter 5.9 of [9]).

The term $\nabla\frac{1}{R}\cdot d\vec{S}_h$ in Eqn. 4 is the solid angle $d\omega$ subtended by the elementary surface element $dS_h(\vec{x})$ at $\vec{y}$, and so we find

$$\varphi_\infty(\vec{y},t) \propto -\int_{S_h} \varphi_m(\vec{x},t) d\omega(\vec{y},\vec{x}). \tag{5}$$

Comprehensive Review Article on Source Modeling

Paper 4

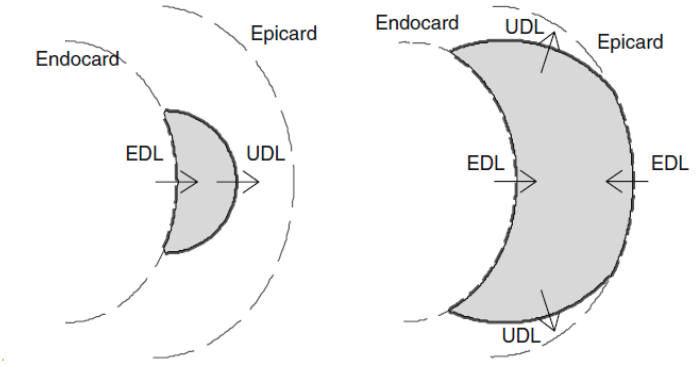
Lead author:	van Oosterom, A	**Year:**	2011
Institution/s:	Radboud University Nijmegen		
Journal:	Basic Electrocardiology		
Reference:	*van Oosterom A. The Equivalent Double Layer; Source Models for Repolarization. In: P. W. Macfarlane, A. van Oosterom, O. Pahlm, P. Kligfield, M. C. Janse and J. Camm, eds. Basic Electrocardiology London: Springer; 2011: 227-246.*		

Contribution to ECG Excellence technology:	Provides the historical overview of cardiac modeling in general and the equivalent dipole layer in particular

Abstract:

The modeling of the electric current sources during depolarization by means of the uniform double layer (UDL) is described. It is linked to the electrophysiology of wave fronts propagating through the myocardium. Some decades ago studies appeared the exploited the equivalence between the actual double layer at the wave fronts and a source description on the heart surface, the surface bounding the myocardium. This source description has been found to be very effective in the inverse determination of the timing of depolarization on the basis of observed body surface potentials, a method now commonly referred to as activation time imaging.

Around the same period, the development of a source model started in which the equivalent cardiac electric generator is expressed in terms of the electric potentials on a surface encompassing the myocardium, similar to the pericardium. In most related studies the unique one-to-one relationship between the voltage on the surface bounding a volume conductor and those on some interior surface, on condition that the surface is closed and that no primary sources are assumed to lie within the inner surface. Inverse methods based on this relationship aim at obtaining a "closer look" at the sources without assuming any a priori knowledge about the nature of these sources. Both source models can be classed being equivalent surface source models (ESS). In the case of the extended UDL variant the current sources are of the double layer type, in the second approach the electric current sources stem from a specification of the potential distribution on the epicardium.



Building on Prior Groundwork

Volume Conductor Modeling

Paper 5

Lead author:	Van Dam, P M	Year:	2005
Institution/s:	Radboud University Nijmegen		
Journal:	Europace		
Reference:	*van Dam, P.M. & van Oosterom, A. (2005). Volume conductor effects involved in the genesis of the P wave. Europace 7, S30-S38.*		

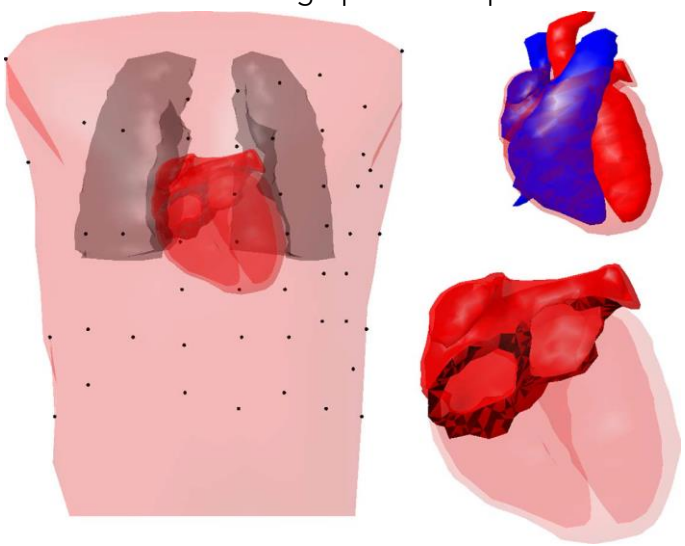
Contribution to ECG Excellence technology:	Investigated the sensitivity of the volume conductor compartments with different conductivity on the atrial signals on the body surface

Abstract:

Aim: To assess the effect of inhomogeneities in the conductivity of different tissues, such as blood and lung tissue, on the body surface potentials generated by atrial electrical activity.

Methods and Results: A 64-lead ECG from a healthy subject was recorded. The subject's geometries of torso, lungs, heart, and blood cavities were derived by magnetic resonance imaging. These geometries were used to construct a numerical volume conductor model. The boundary element method was applied to simulate the potentials on the surface of the thorax generated by the atria. The equivalent

double layer served as the source description during depolarization. Recorded body surface potentials were used as a check on the simulations. Subsequently, the conductivities in the model were varied to determine their influence on P wave morphology and amplitude. The model with realistic conductivity values for blood and lungs produced potentials that closely matched the measured ones (correlation 98%). The subsequent variation of conductivity of blood and lungs revealed a major influence on P wave morphology and amplitude: a mean reduction in amplitude by 42%, with pronounced inter-lead differences.



Conclusion: The inhomogeneities of lungs and atrial blood cavities need to be incorporated in volume conductor models linking atrial electric activity to body surface potentials.

Generation of Activation Using Fastest Route Algorithm

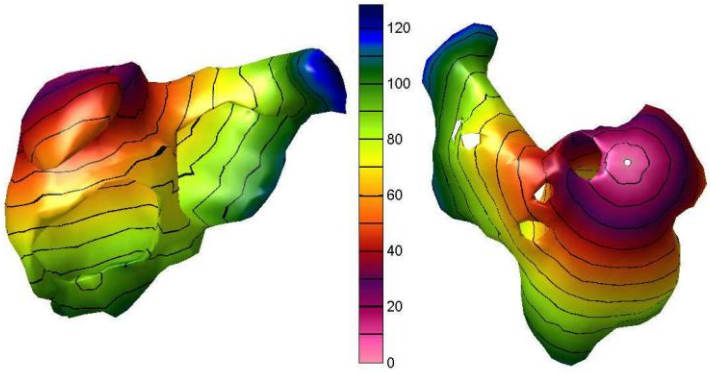
Paper 6

Lead author:	van Oosterom, A	**Year:**	2005
Institution/s:	Radboud University Nijmegen		
Journal:	Computers in Cardiology		
Reference:	*van Oosterom, A. & van Dam, P.M. (2005). The intra-myocardial distance function as used in the inverse computation of the timing of depolarization and repolarization. Computers in Cardiology (A. Murray, Ed.), Vol. 32, 567-570. IEEE Computer Society Press, Lyon, France.*		

Contribution to ECG Excellence technology:	The first use of the shortest path algorithm to compute the activation sequence of the atria

Abstract:

The inverse computation of the timing of depolarization of the ventricular myocytes on the basis of observed body surface potentials has been shown to be feasible. More recently, this method has been extended to the inverse computation of the timing of ventricular repolarization based on the equivalent double layer surface source model (EDL), as well as to atrial activation. The inverse computation of timing constitutes a nonlinear parameter estimation problem, and as such requires an initial estimate. The subsequent iterative solution requires the inclusion of a constraint. This paper introduces novel methods for the handling of both requirements, both based on the intra-myocardial distance function: the shortest distance between any point on the myocardial surface and all other points on the same surface while passing through the myocardium. The effectiveness of the methods is demonstrated in their application to the inverse computation of the timing of depolarization and repolarization of the atria of a healthy subject.



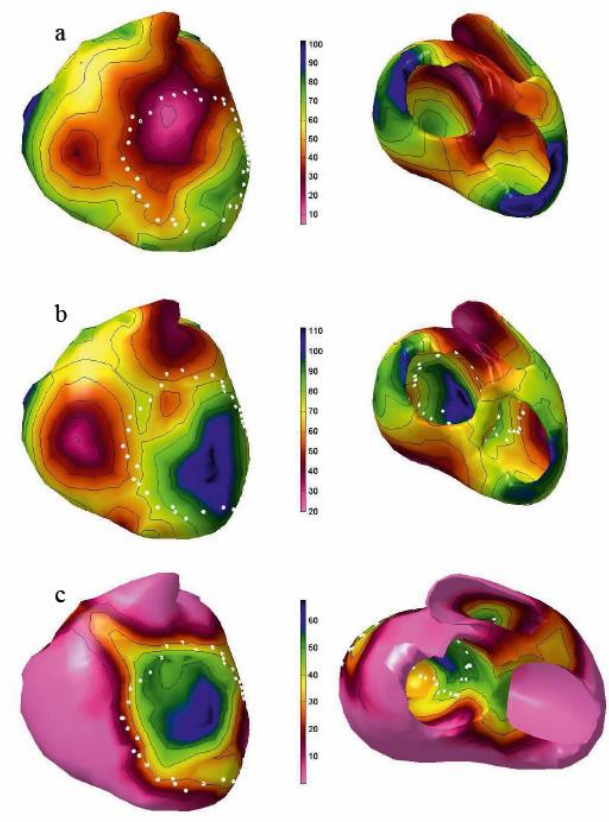
Paper 7

Lead author:	Van Dam, P M	Year:	2007
Institution/s:	Radboud University Nijmegen		
Journal:	IEEE Computer Society Press		
Reference:	*van Dam, P.M., Oostendorp, T.F., & van Oosterom, A. (2007). Simulating ECG changes during acute myocardial infarction. Computers in Cardiology (A. Murray, Ed.), Vol. 34. IEEE Computer Society Press, Durham, NC, USA.*		

Contribution to ECG Excellence technology:	Ability to change the activation sequence by locally reducing the propagation velocity of the activation wave

Abstract:

In this paper the changes in ECG waveforms during the first 20 minutes of an ischemic event are studied in a simulation model. A new method, based on the shortest path algorithm, is introduced for simulating the effects of the reduced propagation velocity within an ischemic zone on the timing of the depolarization sequence throughout the entire myocardium and the resulting ECG changes.



Simulated ischemic activation sequences and the difference in timing compared to the reference activation timing (Figure 1). Panel a: Activation sequence with reduced propagation velocity of 10% in the ischemic region. Panel b: As in panel a; velocity reduced by 25%. Panel c; the difference between the timing in panel b and the reference timing shown in Figure 1. All panels, left: anterior view; right: posterior-basal view (In panel c the right view has been rotated such that the septum is visible). Isochrones are drawn at 10 ms intervals. The white dots indicate the border of the ischemic area.

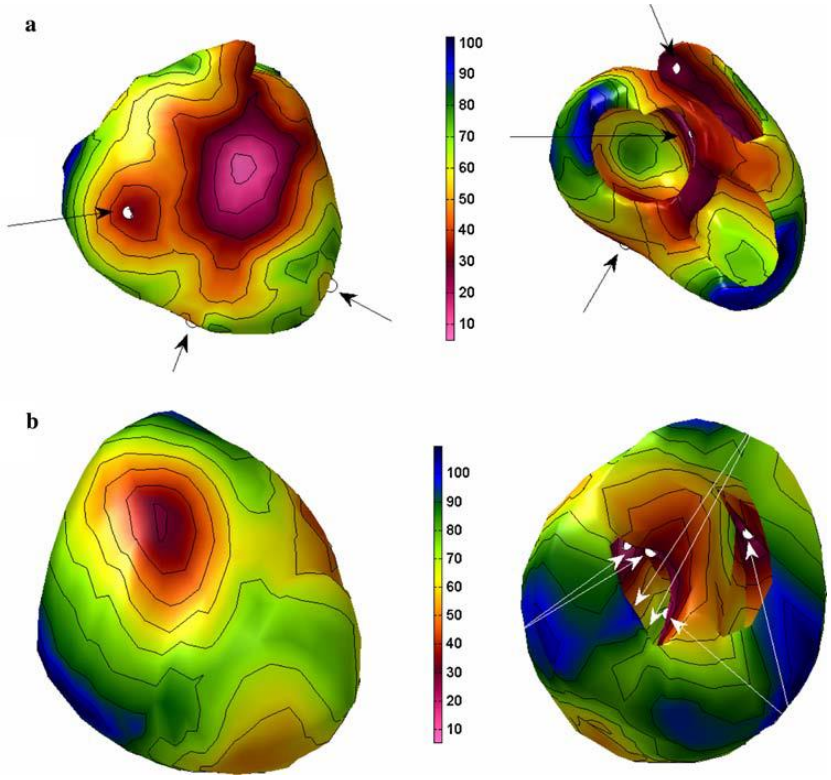
Paper 8

Lead author:	Van Dam, P M	Year:	2009
Institution/s:	Radboud University Nijmegen		
Journal:	Medical & Biological Engineering & Computing		
Reference:	*van Dam, P.M., Oostendorp, T.F., & van Oosterom, A. Application of the fastest route algorithm in the interactive simulation of the effect of local ischemia on the ECG. Medical & Biological Engineering & Computing 2009;47(1):11-20.*		

Contribution to ECG Excellence technology:	Model to model comparison of the use of eth fastest route algorithm with normal and reduced propagation velocity

Abstract:

A method is described to determine the effect on the ECG of a reduced propagation velocity within an ischemic zone. The method was designed to change the activation sequence throughout the ventricles interactively, i.e. with a response time in the order of a second. The timing of ventricular ischemic activation was computed by using the fastest route algorithm, based on locally reduced values of the propagation velocities derived from a standard, normal activation sequence. The effect of these local reductions of the velocities on the total activation sequence, as well as the changes in the electrocardiogram that these produce, are presented.



iECG (ECG Mapping) Validation

Human

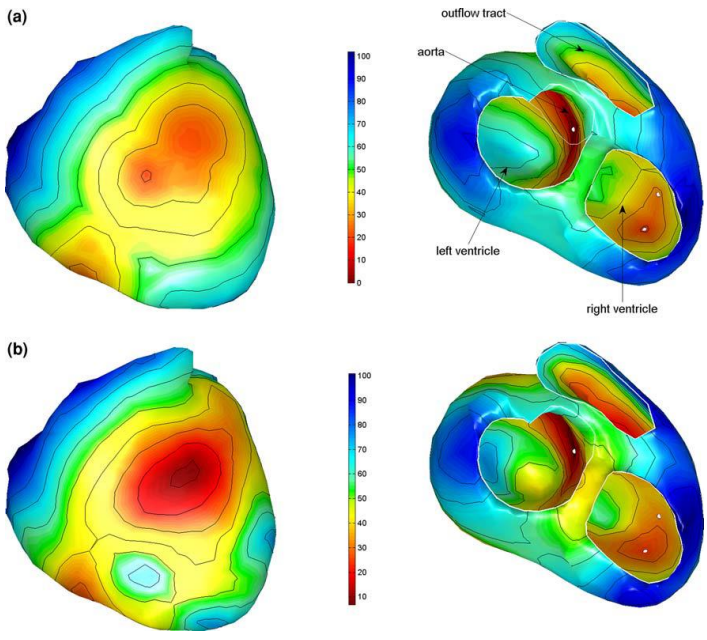
Paper 9

Lead author:	van Dam, P M	**Year:**	2009
Institution/s:	Radboud University Nijmegen		
Journal:	Annals of Biomedical Engineering		
Reference:	*van Dam, P.M., Oostendorp, T.F., Linnenbank, A.C., & van Oosterom, A. Non-Invasive Imaging of Cardiac Activation and Recovery. Annals of Biomedical Engineering 2009;37(9):1739-56*		

Contribution to ECG Excellence technology:	Feasibility study to localize the multiple breakthroughs of the His-Purkinje system and estimate the resulting activation and recovery sequence

Abstract:

The sequences of activation and recovery of the heart have physiological and clinical relevance. We report on progress made over the last years in the method that images these timings based on an equivalent double layer on the myocardial surface serving as the equivalent source of cardiac activity, with local transmembrane potentials (TMP) acting as their strength. The TMP wave forms were described analytically by timing parameters, found by minimizing the difference between observed body surface potentials and those based on the source description. The parameter estimation procedure involved is non-linear, and consequently requires the specification of initial estimates of its solution. Those of the timing of depolarization were based on the fastest route algorithm, taking into account properties of anisotropic propagation inside the myocardium. Those of recovery were based on electrotonic effects. Body surface potentials and individual geometry were recorded on: a healthy subject, a WPW patient and a Brugada patient during an Ajmaline provocation test. In all three cases, the inversely estimated timing agreed entirely with available physiological knowledge. The improvements to the inverse procedure made are attributed to our use of initial estimates based on the general electrophysiology of propagation. The quality of the results and the required computation time permit the application of this inverse procedure in a clinical setting.



Paper 10

Lead author:	Boonstra	Year:	2020
Institution/s:	UMC Utrecht		
Journal:	Circulation A&E		
Reference:	*Boonstra MJ Roudijk RW, Brummel R., Kassenberg W, Blom, LJ, Oostendorp TF, te Riele ASJM, van der Heijden JF, Asselbergs FW, Loh P, van Dam P.M. (2020). Circulation A&E. (submitted)*		

Contribution to ECG Excellence technology:	Human validation study on the intrinsic cardiac activation estimation

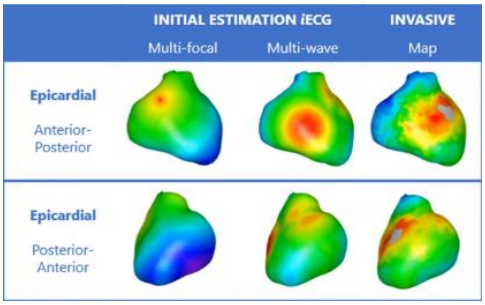
Abstract:

Background: Inverse electrocardiography (iECG) estimates cardiac electrical activity from measured body surface potentials maps (BSPM). In individuals at risk for cardiomyopathy, non-invasive estimation of normal ventricular activation may provide valuable information to identify onset of disease or aid risk stratification in order to prevent sudden cardiac death. However, multiple activation wavefronts occurring during normal (His-Purkinje mediated) ventricular activation, complicate iECG. Previously, multi-focal iECG was developed to estimate normal ventricular activation. However, to accurately mimic the effect of the His-Purkinje system on ventricular activation, a novel multi-wave iECG method was developed. In this novel method, the initial estimation of the ventricular activation sequence is based on a combination of waveforms initiated from His-Purkinje associated endocardial anatomical regions instead of one like in multi-focal iECG. This study aimed to compare the performance of two iECG methods in His-Purkinje mediated ventricular activation.

Methods: Multi-focal iECG and multi-wave iECG were tested in four patients undergoing invasive electro-anatomical mapping (EAM) during normal ventricular activation. In each subject, 67-electrode BSPM were recorded during His-Purkinje mediated ventricular activation and used as input for both iECG methods. The iECG estimated local activation timing (LAT) maps were compared to invasive endocardial and epicardial LAT maps.

Results: Median [range] epicardial inter-map correlation coefficient (CC) between invasive LAT maps and estimated multi-focal iECG versus multi-wave iECG was 0.31[-0.23,0.83] versus 0.61[0.41,0.91] for His-Purkinje mediated ventricular activation. Endocardial inter-map CC was 0.22[-0.13,0.64] respectively 0.54[0.19,0.81].

Conclusion: Multi-wave iECG shows improved performance compared to multi-focal iECG for the estimation of normal His-Purkinje mediated ventricular activation, especially in narrow QRS complexes. Future research aims to implement the effects of conduction defects(?), scar and fibrotic tissue into the iECG method.



Porcine

Paper 11

Lead author:	Oosterhoff, P	**Year:**	2016
Institution/s:	Radboud University Nijmegen		
Journal:	Circulation: Arrhythmia and Electrophysiology		
Reference:	*Oosterhoff, P., Meijborg, VMF., van Dam, P.M., van Dessel, PFHM., Belterman CNW., Streekstra, GJ., et al. Experimental Validation of Noninvasive Epicardial and Endocardial Activation Imaging. Circulation: Arrhythmia and Electrophysiology. 2016;9(8):e004104.*		

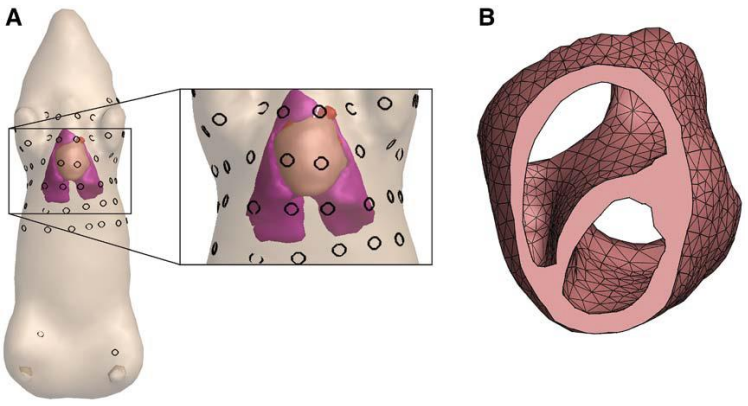
Contribution to ECG Excellence technology:	Validation of the iECG methodology in porcine measurements using Body surface mapping and a porcine specific model

Abstract:

Background: Noninvasive imaging of cardiac activation before ablation of the arrhythmogenic substrate can reduce electrophysiological procedure duration and help choosing between an endocardial or epicardial approach. A noninvasive imaging technique was evaluated that estimates both endocardial and epicardial activation from body surface potential maps. We performed a study in isolated and in situ pig hearts, estimating activation from body surface potential maps during sinus rhythm and localizing endocardial and epicardial stimulation sites.

Methods and Results: From 3 Langendorff-perfused pig hearts, 180 intramural unipolar electrograms were recorded during sinus rhythm and ectopic activation, together with pseudo–body surface potential map ECGs in 2 of them. From 4 other anesthetized pigs, 64-lead body surface potential maps were recorded during sinus rhythm and ventricular stimulation from 27 endocardial and epicardial sites. The ventricular activation pattern was computed from the recorded QRS complexes. For both Langendorff-perfused hearts, the calculated epicardial and endocardial activation patterns showed good qualitative correspondence to the patterns obtained with needle electrodes. Absolute timing difference for sinus rhythm was 10±5 and 11±8 ms respectively, and for ectopic activation 6±5 and 7±6 ms, respectively. Calculated activation for the in situ hearts in sinus rhythm was similar to patterns recorded in Langendorff-perfused hearts. During stimulation, the distance between the stimulation site and calculated site of earliest activation was 18 (15–27) mm, and 23 of 27 stimulation sites were correctly mapped to either endocardium or epicardium.

Conclusions: Noninvasive activation imaging is able to determine earliest ventricular activation and discriminate endocardial from epicardial origin of activation with clinically relevant accuracy.



Improving the understanding of the ECG

Model study

Paper 12

Lead author:	Erem, B	Year:	2014
Institution/s:	North Eastern University , Boston		
Journal:	IEEE Transactions on Medical Imaging		
Reference:	*Erem, B., van Dam, P.M., Brooks, D.H. Identifying Model Inaccuracies and Solution Uncertainties in Noninvasive Activation-Based Imaging of Cardiac Excitation Using Convex Relaxation. IEEE Transactions on Medical Imaging 2014; 33(4):902-912*		

Contribution to ECG Excellence technology:	Study to regularize the optimization process in a different way

Abstract:

Noninvasive imaging of cardiac electrical function has begun to move towards clinical adoption. Here, we consider one common formulation of the problem, in which the goal is to estimate the spatial distribution of electrical activation times during a cardiac cycle. We address the challenge of understanding the robustness and uncertainty of solutions to this formulation. This formulation poses a nonconvex, nonlinear least squares optimization problem. We show that it can be relaxed to be convex, at the cost of some degree of physiological realism of the solution set, and that this relaxation can be used as a framework to study model inaccuracy and solution uncertainty. We present two examples, one using data from a healthy human subject and the other synthesized with the ECGSIM software package. In the first case, we consider uncertainty in the initial guess and regularization parameter. In the second case, we mimic the presence of an ischemic zone in the heart in a way which violates a model assumption. We show that the convex relaxation allows understanding of spatial distribution of parameter sensitivity in the first case, and identification of model violation in the second.

Anatomical Model Creation

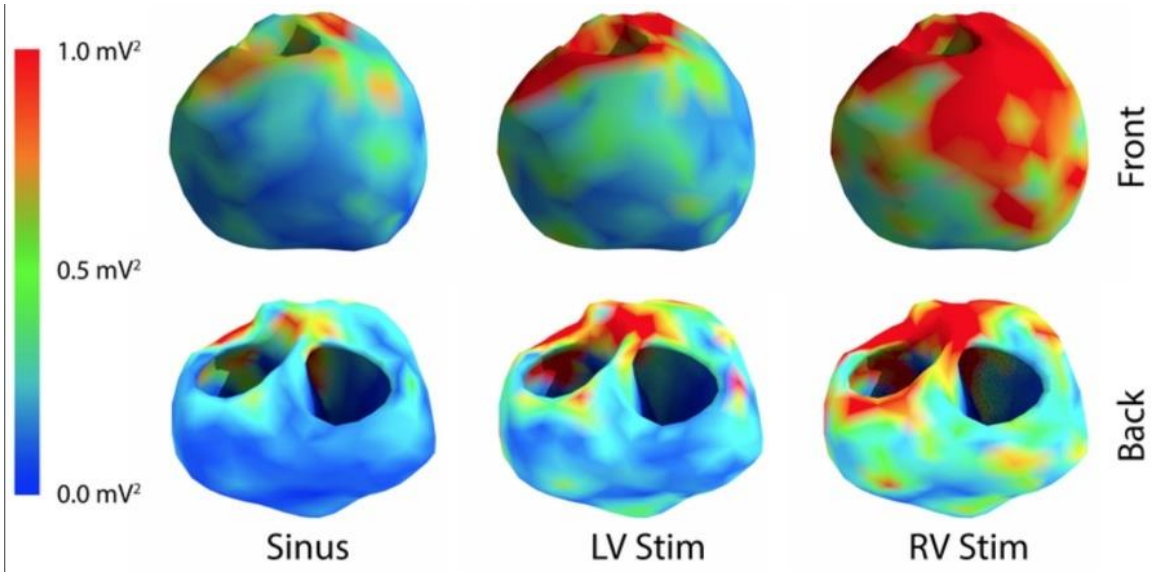
Paper 13

Lead author:	Tate, J.D	**Year:**	2010
Institution:	SCI Institute, Salt lake City, Utah University , USA		
Journal:	Computers in Cardiology		
Reference:	*Tate, J.D., Zemzemi, N., Good, W.W., van Dam, P.M., Brooks, D.H. & MacLeod, R.S. Effect of Segmentation Variation on ECG Imaging. Computers in Cardiology. (2010). 2018;45.*		

Contribution to ECG Excellence technology:	Study that investigated the influence of model uncertainties on the iECG methods

Abstract:

ECG imaging (ECGI) is the process of calculating electrical cardiac activity from body surface recordings from the geometry and conductivity of the torso volume. A key first step to create geometric models for ECGI and a possible source of considerable variability is to segment the surface of the heart. We hypothesize that this variation in cardiac segmentation will produce variation in the computed ventricular surface potentials from ECGI. To evaluate this hypothesis, we leveraged the resources of the Consortium for ECG Imaging (CEI) to carry out a comparison of ECGI results from the same body surface potentials and multiple ventricular segmentations. We found that using the different segmentations produced variability in the computed ventricular surface potentials. Not surprisingly, locations of greater variance in the computed potential correlated to locations of greater variance in the segmentations, for example near the pulmonary artery and basal anterior left ventricular wall. Our results indicate that ECGI may be more sensitive to segmentation errors on the anterior epicardial surface than on other areas of the heart.



Paper 14

Lead author:	Van Dam, P M	Year:	2015
Institution/s:	University of California Los Angeles		
Journal:	Journal of Electrocardiology		
Reference:	*van Dam, P.M., Gordon, J.P., Laks, M., & Boyle, N.G. Development of new anatomy reconstruction software to localize cardiac isochrones to the cardiac surface from the 12 lead ECG. Journal of Electrocardiology. 2015, 48(6): 959-965.*		

Contribution to ECG Excellence technology:	Introduction of the software with which all volume conductor models are created.

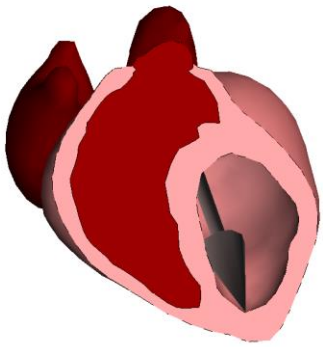
Abstract:

Non-invasive electrocardiographic imaging (ECGI) of the cardiac muscle can help the pre-procedure planning of the ablation of ventricular arrhythmias by reducing the time to localize the origin. Our non-invasive ECGI system, the cardiac isochrone positioning system (CIPS), requires non-intersecting meshes of the heart, lungs and torso. However, software to reconstruct the meshes of the heart, lungs and torso with the capability to check and prevent these intersections is currently lacking. Consequently the reconstruction of a patient specific model with realistic atrial and ventricular wall thickness and incorporating blood cavities lungs and torso usually requires additional several days of manual work. Therefore new software was developed that checks and prevents any intersections, and thus enables the use of accurate reconstructed anatomical models within CIPS.

In this preliminary study we investigated the accuracy of the created patient specific anatomical models from MRI or CT. During the manual segmentation of the MRI data the boundaries of the relevant tissues are determined. The resulting contour lines are used to automatically morph reference meshes of the heart, lungs or torso to match the boundaries of the morphed tissue. Five patients were included in the study; models of the heart lungs and torso were reconstructed from standard cardiac MRI images. The accuracy was determined by computing the distance between the segmentation contours and the morphed meshes.

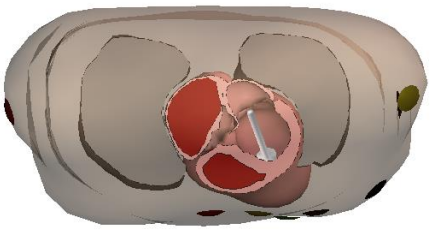
The average accuracy of the reconstructed cardiac geometry was within 2 mm with respect to the manual segmentation contours on the MRI images. Derived wall volumes and left ventricular wall thickness were within the range reported in literature. For each reconstructed heart model the anatomical heart axis was computed using the automatically determined anatomical landmarks of the left apex and the mitral valve. The accuracy of the reconstructed heart models were well within the accuracy of the used medical image data (pixel size < 1.5 mm). For the lungs and torso the number of triangles in the mesh were reduced, thus decreased the accuracy of the reconstructed mesh.

A novel software tool has been introduced able to reconstruct accurate cardiac anatomical models from MRI or CT within only a few hours. This new anatomical reconstruction tool might reduce the modeling errors within the cardiac isochrone positioning system and thus enable the clinical application of CIPS to localize the PVC/VT focus to the ventricular myocardium from only the standard 12 lead ECG

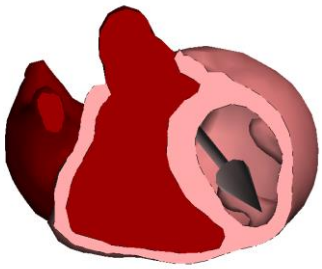


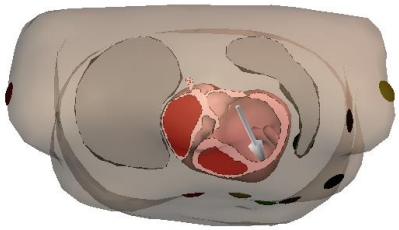
AP view

frontal plane



horizontal plane





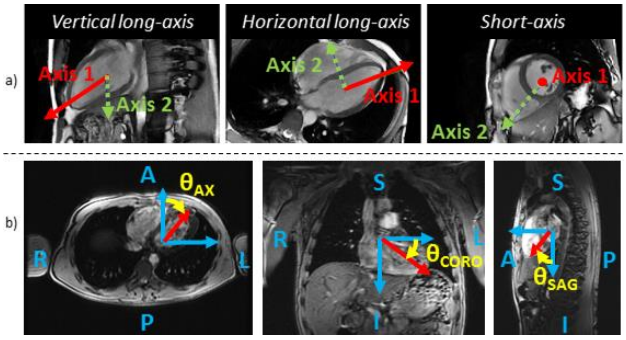
Paper 15

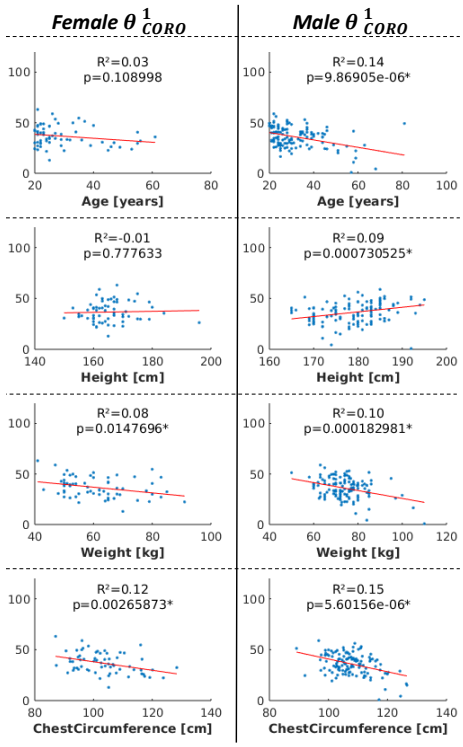
Lead author:	*Odille F*	Year:	2017
Institution/s:	IADI, INSERM and Université de Lorraine, Nancy, France		
Journal:	Computing in Cardiology Conference		
Reference:	*Odille F, Liu S, Dam PMv and Felblinger J. Statistical Variations of Heart Orientation in Healthy Adults. Computing in Cardiology. 2017;44:1-4.*		

Contribution to ECG Excellence technology:	Determine parameters to position and orient the heart without the need of cardiac imaging like MRI or CT

Abstract:

The orientation of the heart in the chest impacts the shape and amplitude of surface ECG signals. It is also key information in electrocardiographic imaging (ECGI), where a model of the heart and torso is required. In this study we seek to analyze statistical relations between heart orientation and several easily available patient characteristics. Heart orientation data were obtained from an MRI database of 185 healthy adults. Relations with sex, height, weight (collected from case reports forms) and chest circumference (extracted from the images) were analyzed using univariate and multivariate linear regression. Chest circumference was found to be the best single predictor of heart orientation, and simple formulas were determined for its estimation. The proposed heart orientation statistical model might be used for selecting a torso/heart model from an existing database; this approach might allow ECGI techniques to be integrated into an ECG device.





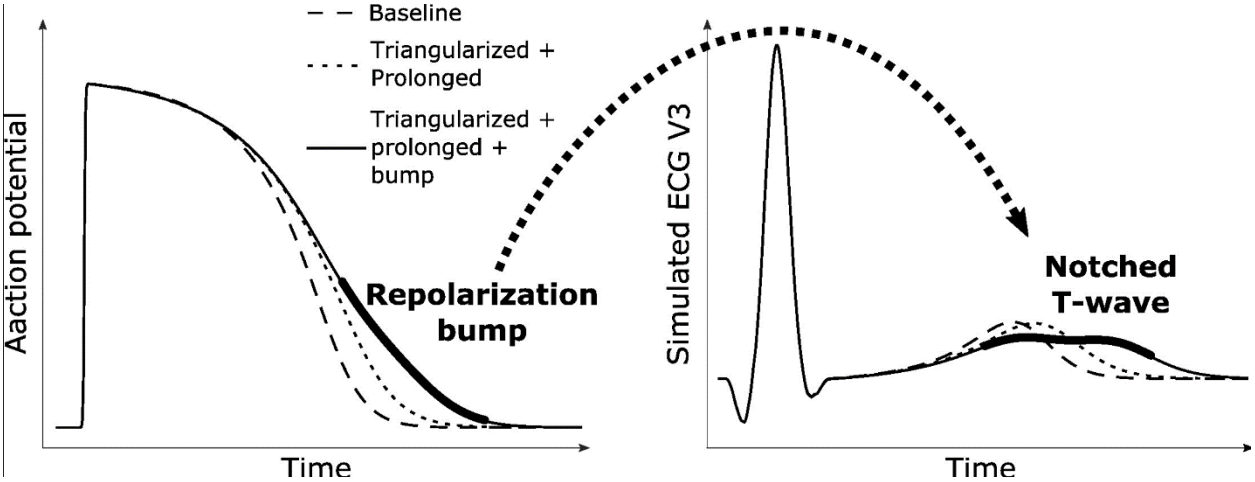
Paper 16

Lead author:	Galeotti, L	Year:	2015
Institution/s:	Radboud University Nijmegen, Food & Drug Administration		
Journal:	Journal of Electrocardiology		
Reference:	*Galeotti, L., van Dam, P.M., Johannesen, L., Vicente, J., & Strauss, D.G. Computer simulations to investigate the causes of T-wave notching. Journal of Electrocardiology. 2015; 48(6):927-32.*		

Contribution to ECG Excellence technology:	The EDL froward model was used to simulate relevant repolarization changes, supporting the understanding of drug influences on the T-wave morphology

Abstract:

Drugs that cause strong hERG potassium channel block (e.g., dofetilide, quinidine) cause T-wave notching. It has been suggested that this is due to prolongation of mid-myocardial (M) cells' action potential duration relative to endocardial and epicardial cells. However, the role of M cells in intact human hearts is debated. We simulated 2025 electrocardiograms representing changes in ventricular action potentials using the equivalent double layer mode that does not include M-cells. Action potential changes included prolongation, triangularization, squaring, and bumps in late repolarization, which have been observed experimentally and in single cell models with block of the hERG potassium channel. Changes were applied globally and spatially dispersed. Action potential bumps (slowing in late repolarization) produced T-wave notching similar to that observed clinically in healthy subjects receiving dofetilide or quinidine. Conversely, all other action potential changes (i.e., prolongation, triangularization, squaring), either global or spatially dispersed, resulted in T-wave changes, but did not cause T-wave notching. This study demonstrates that M-cells are not required to simulate T-wave notching.



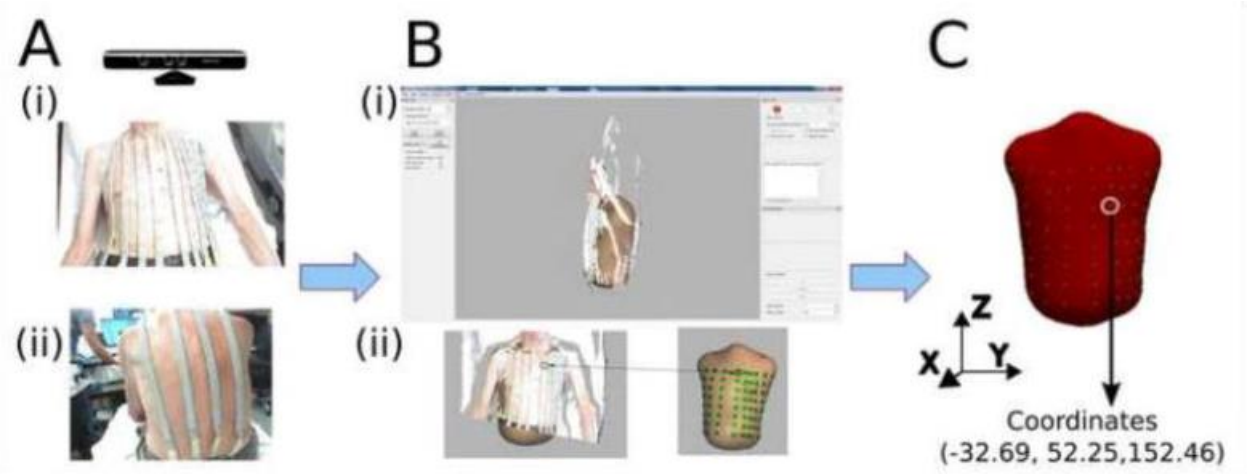
Paper 17

Lead author:	Perez-Alday EA	Year:	2018
Institution/s:	Oregon Health and Science University, University of Oregon		
Journal:	Journal of Electrocardiology		
Reference:	*Perez-Alday, E.A., Thomas, J.A., Kabir, M., Sedaghat, G., Rogovoy, N., van Dam, E., van Dam, P.M., Woodward, W., Fuss, C., Ferencik, M. & Tereshchenko, L.G. Torso geometry reconstruction and body surface electrode localization using three-dimensional photography. Journal of Electrocardiology. 2018;51(1):60-7.*		

Contribution to ECG Excellence technology:	The 3D camera, used to localize the ECG electrode positions system was tested in this study

Abstract:

We conducted a prospective clinical study (n = 14; 29% female) to assess the accuracy of a three-dimensional (3D) photography-based method of torso geometry reconstruction and body surface electrodes localization. The position of 74 body surface electrocardiographic (ECG) electrodes (diameter 5 mm) was defined by two methods: 3D photography, and CT (marker diameter 2 mm) or MRI (marker size 10 × 20 mm) imaging. Bland-Altman analysis showed good agreement in X (bias − 2.5 [95% limits of agreement (LoA) − 19.5 to 14.3] mm), Y (bias -0.1 [95% LoA − 14.1 to 13.9] mm), and Z coordinates (bias − 0.8 [95% LoA − 15.6 to 14.2] mm), as defined by the CT/MRI imaging, and 3D photography. The average Hausdorff distance between the two torso geometry reconstructions was 11.17 ± 3.05 mm. Thus, accurate torso geometry reconstruction using 3D photography is feasible. Body surface ECG electrodes coordinates as defined by the CT/MRI imaging, and 3D photography, are in good agreement.



Localization of Premature Ventricular Complexes

Paper 18

Lead author:	van Dam, P M	**Year:**	2013
Institution/s:	University of California Los Angeles		
Journal:	Journal of Electrocardiology		
Reference:	*van Dam, P.M., Tung, R., Shivkumar, K., & Laks, M. Quantitative Localization of Premature Ventricular Contractions using Myocardial Activation ECGI from the Standard 12-Lead Electrocardiogram Journal of Electrocardiology 2013; 46(6):574-9.*		

Contribution to ECG Excellence technology:	Feasibility study to localize PVC origins to the cardiac anatomy using an VCG based inverse solver

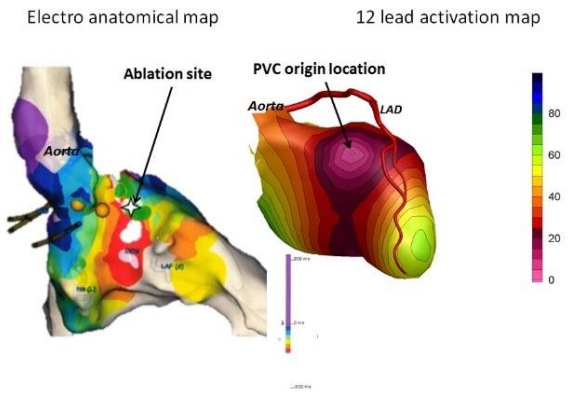
Abstract:

Background. The precise localization of the site of origin of a premature ventricular contractions (PVC) prior to ablation would facilitate the planning and execution of the electrophysiological procedure. Current electrocardiographic imaging (ECGI) techniques require body surface maps, a costly and complex procedure, that requires as many as 256 leads to localize the PVC origin. We developed and tested a novel myocardial activation based ECGI technique utilizing the readily available 12-lead ECG to localize the PVC origin.

Methods. The major components of the 12-lead ECGI method are: the source model, proximity effect and spatial orientation, volume conductor, and patient specific model of the heart, lungs, and thorax as derived from magnetic resonance imaging (MRI). For the PVC origin localization, the fastest route algorithm is used on patient specific models created by developed morphing software. PVC localization by 12-lead ECGI was correlated to the site of successful ablation.

Results. Seven patients that underwent electrophysiological mapping and ablation of PVCs were studied. All patients (7/7) had accurate prediction of the PVC origin. However in two patients, no specific MRI was used for localization that resulted in an incorrect switch between the RV free wall and septum of the RVOT. With patient-specific models, these latter two cases would likely be localized correctly.

Conclusions. This feasibility study of a novel myocardial activation-based ECGI using only the standard 12-lead ECG shows promise to localize the origin of PVC. This ECGI method yields activation estimates of isochrones on both ventricles from which the PVC origin location is derived. This method has the capability to localize the PVC from any part of the ventricular endocardium, intra-myocardium or epicardium.



Paper 19

Lead author:	van Dam, P M	Year:	2014
Institution/s:	Radboud University Nijmegen, University of California Los Angeles		
Journal:	Journal of Electrocardiology		
Reference:	*van Dam, P.M., Gordon, J.P., & Laks, M: Sensitivity of CIPS-computed PVC location to measurement errors in ECG electrode position: the need for the 3D Camera. Journal of Electrocardiology 2014 11; 47(6):788-93.*		

Contribution to ECG Excellence technology:	Tested the inverse system sensitivity to ECG electrode placement errors in the localization of the onset of a PVC

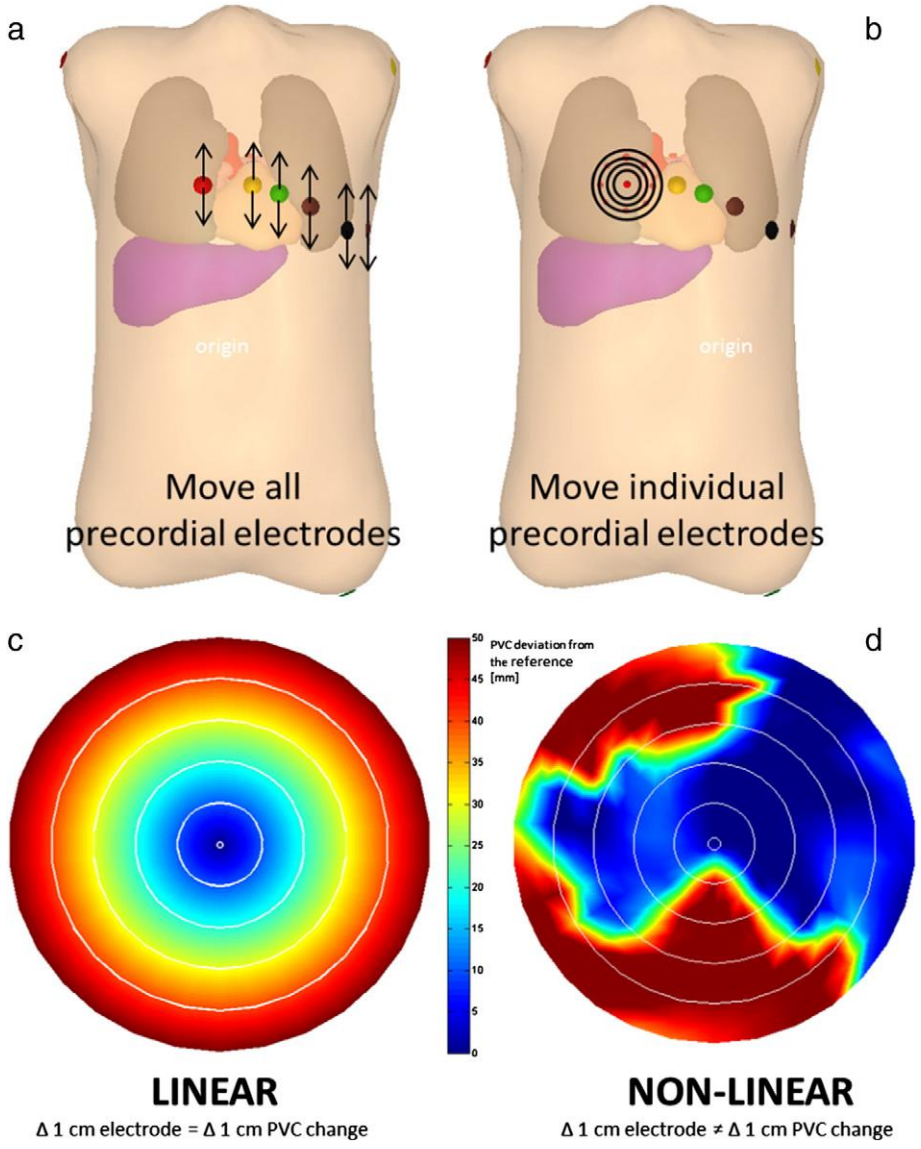
Abstract:

Background: The Cardiac Isochrone Positioning System (CIPS) is a non-invasive method able to localize the origins of PVCs,VT andWPWfromthe 12 lead ECG. The CIPSmodel integrates a standard 12-lead ECG with an MRI derived model of the heart, lungs, and torso in order to compute the precise electrical origin of a PVC from within the myocardium. To make these calculations, CIPS uses virtually represented ECG electrode positions. These virtual electrode positions, however, are currently assumed to represent the standard 12 lead positions in the modelwithout taking into account the actual, anatomical locations on a patient. The degree of error introduced into the CIPS model by movement of the virtual electrodes is unknown. Therefore, we conducted a model-based study to determine the sensitivity of CIPS to changes in its virtually represented ECG electrode positions.

Methods: Previously, CIPS was tested on 9 patients undergoing PVC ablation, producing a precise myocardial PVC location for each patient. These initial results were used as controls in two different simulation experiments. The first moved all virtual precordial leads in CIPS simultaneously up and down to recalculate a PVC origin. The second moved each virtual precordial lead individually, using 8 points on multiple concentric circles of increasing radius to recalculate a PVC origin. The distance of the newly calculated PVC origin from the control origin was used as a metric.

Results: Moving either all electrodes simultaneously or each V1-6 precordial electrode independently resulted in non-linear and unpredictable shifts of the CIPS-computed PVC origin. Simultaneously moving all V1-6 precordial electrodes by 10 mm increments produced a shift in CIPS-computed PVC origin between 0 and 62 mm. Independently moving an electrode, a shift of more than 10 mm resulted in an unpredictable CIPS-computed PVC origin relocation between 0 and 40 mm. The effect of moving the virtual electrodes on CIPS modeling more pronounced the closer the virtual electrode was positioned to the actual PVC origin. Conclusions: Slight changes in the virtual positions of the V1-6 precordial electrodes produce marked, non-linear and unpredictable shifts in the CIPS-computed PVC origin. Thus, any variation in the physical ECG electrode placement on a patient can result in significant error within the CIPS model. These large errors would make CIPS useless and underscore the need for accurate, patient specific measurement of electrode position relative to the patient specific

torso geometries. A potential solution to this problem could be the introduction of a 3D camera to incorporate accurate measurement of physical electrode placement into the CIPS model. Since the 3D camera software integrates the 3D imaged position of the electrode with the MRI derived torso model, it is conveniently incorporated in the next generation CIPS software to decrease the errors in modeled location of the electrodes. Thus, the 3D camera will be the IIIrd component of the CIPS to increase its accuracy in PVC, VT, and WPW localization.



Paper 20

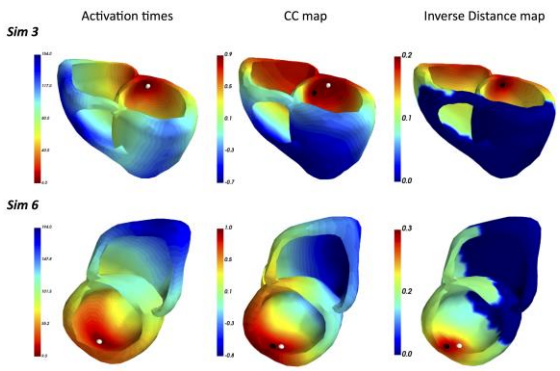
Lead author:	Potyagaylo, D	Year:	2016
Institution/s:	Karlsruhe Institute of Technology		
Journal:	IEEE Transactions on Biomedical Engineering.		
Reference:	*Potyagaylo, D., Doessel, O., & van Dam, P.M. Influence of Modeling Errors on the Initial Estimate for Nonlinear Myocardial Activation Times Imaging Calculated with Fastest Route Algorithm. IEEE Transactions on Biomedical Engineering. 2016; 99.*		

Contribution to ECG Excellence technology:	Testing the fastest route based algorithm to localize pacing sites. This can be used in localizing the LV and RV lead positions during implant

Abstract:

Although model-based solution strategies for the ECGI were reported to deliver promising clinical results, they strongly rely on some a priori assumptions, which do not hold true for many pathological cases. The fastest route algorithm (FRA) is a well-established method for noninvasive imaging of ectopic activities. It generates test activation sequences on the heart and compares the corresponding test body surface potential maps (BSPMs) to the measured ones. The test excitation propagation patterns are constructed under the assumption of a global conduction velocity in the heart, which is violated in the cardiac resynchronization (CRT) patients.

In the present work, we propose to apply the dynamic time warping (DTW) to the test and measured ECGs before measuring their similarity. The warping step is a non-linear pattern matching that compensates for local speed-ups and delays in the temporal sequences, while aligning them in an optimal way with respect to a distance function. To evaluate benefits of the temporal warping for FRA-based BSPMs, we considered three scenarios. In the first setting, a simplified simulation example was constructed to illustrate the temporal warping and display the resulting distance map. Then, we applied the proposed method to eight BSPMs produced by realistic ectopic activation sequences and compared its performance to FRA. Finally, we assessed localization accuracy of both techniques in ten CRT patients. For each patient, we noninvasively imaged two paced ECGs: from left- and right ventricular implanted leads. In all scenarios, FRA-DTW outperformed FRA in terms of localization accuracy. For the clinical cases, the distance errors were reduced from 16 (8-23) mm to 5 (2-10) mm for all pacings, from 15 (11-25) to 8 (3-13) mm in the left, and from 19 (6-23) to 4 (2-8) mm in the right ventricle, respectively. The obtained results suggest the ability of temporal ECG warping to compensate for an in-homogeneous conduction profile, while retaining computational efficiency intrinsic to FRA.



Paper 21

Lead author:	van Dam, P M	Year:	2016
Institution/s:	Radboud University Nijmegen, University of California Los Angeles		
Journal:	Europace		
Reference:	*van Dam, Peter M., Boyle, N.G., Laks, M.M., & Tung, R. Localization of premature ventricular contractions from the papillary muscles using the standard 12-lead electrocardiogram: a feasibility study using a novel cardiac isochrone positioning system. Europace. 2016;18(suppl 4):iv16-iv22*		

Contribution to ECG Excellence technology:	Human validation study on localization of the PVC onset papillary muscles, cardiac structures which are very difficult to map

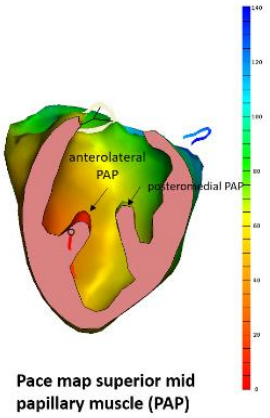
Abstract:

Aims: The precise localization of the site of origin of a premature ventricular contraction (PVC) prior to ablation can facilitate the planning and execution of the electrophysiological procedure. In clinical practice, the targeted ablation site is estimated from the standard 12-lead ECG. The accuracy of this qualitative estimation has limitations, particularly in the localization of PVCs originating from the papillary muscles. Clinical available electrocardiographic imaging (ECGi) techniques that incorporate patient-specific anatomy may improve the localization of these PVCs, but require body surface maps with greater specificity for the epicardium. The purpose of this report is to demonstrate that a novel Cardiac Isochrone Positioning System (CIPS) program can accurately detect the specific location of the PVC on the papillary muscle using only a 12-lead ECG.

Methods: CIPS uses three components: 1) endocardial and epicardial cardiac anatomy and torso geometry derived from MRI, 2) the patient specific electrode positions derived from an MRI model registered 3D image and 3) the 12 lead ECG. CIPS localizes the PVC origin by matching the anatomical isochrone vector with the ECG vector. The predicted PVC origin was compared to the site of successful ablation or stimulation.

Results: Three patients who underwent electrophysiological mapping and ablation of PVCs originating from the papillary muscles were studied. CIPS localized the PVC origin for all three patients to the correct papillary muscle and, specifically to the base, mid or apical region.

Conclusion: A simplified form of ECGi utilizing only 12 standard electrocardiographic leads may facilitate accurate localization of the origin of papillary muscle PVCs.



Pace map superior mid papillary muscle (PAP)

Paper 22

Lead author:	Misra, S	Year:	2018
Institution/s:	Radboud University Nijmegen		
Journal:	Journal of Electrocardiology		
Reference:	*Misra S, van Dam, P.M., Chrispin J, Assis F, Keramati A, Kolandaivelu A, et al. Initial validation of a novel ECGI system for localization of premature ventricular contractions and ventricular tachycardia in structurally normal and abnormal hearts. Journal of Electrocardiology. 2018;51(5):801-8.*		

Contribution to ECG Excellence technology:	Clinical validation of the inverse technology to localize the onset of a PVC/VT to the cardiac anatomy

Abstract:

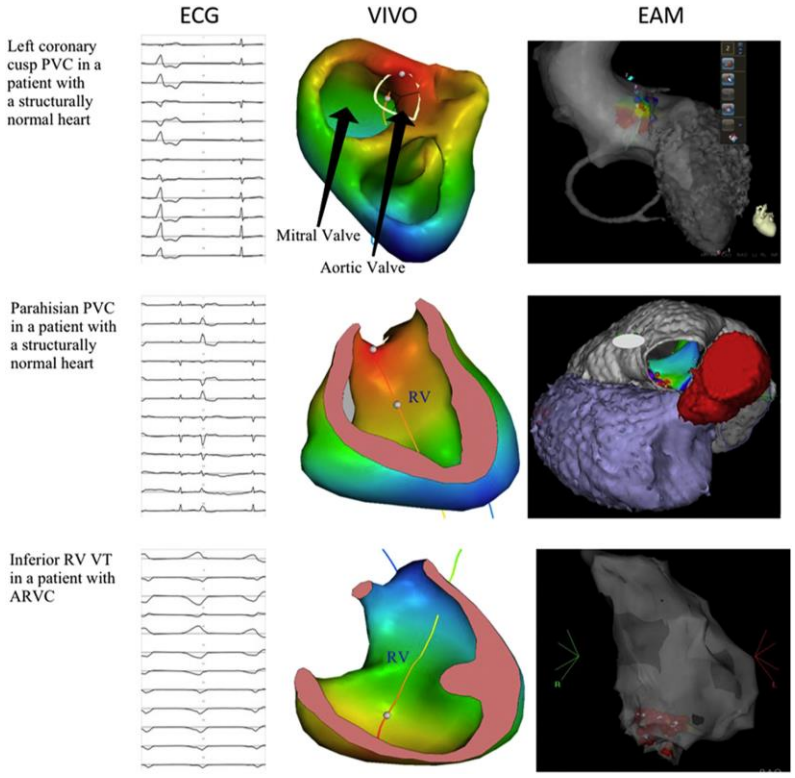
Background: Viewinto Ventricular Onset (VIVO) is a novel ECGI systemthat uses 3D body surface imaging, myocardial CT/MRI, and 12 lead ECG to localize earliest ventricular activation through analysis of simulated and clinical vector cardiograms.

Objective: To evaluate the accuracy of VIVO for the localization of ventricular arrhythmias (VA).

Methods: In twenty patients presenting for catheter ablation of VT [8] or PVC [12], VIVO was used to predict the site earliest activation using 12 lead ECG of the VA. Results were compared to invasive electroanatomic mapping (EAM).

Results: A total of 22 PVC/VT morphologies were analyzed using VIVO. VIVO accurately predicted the location of the VA in 11/13 PVC cases and 8/9 VT cases. VIVO correctly predicted right vs left ventricular foci in 20/22 cases.

Conclusion: View into Ventricular Onset (VIVO) can accurately predict earliest activation of VA, which could aid in catheter ablation, and should be studied further.



Simulation of Conduction Disorders in the ECG

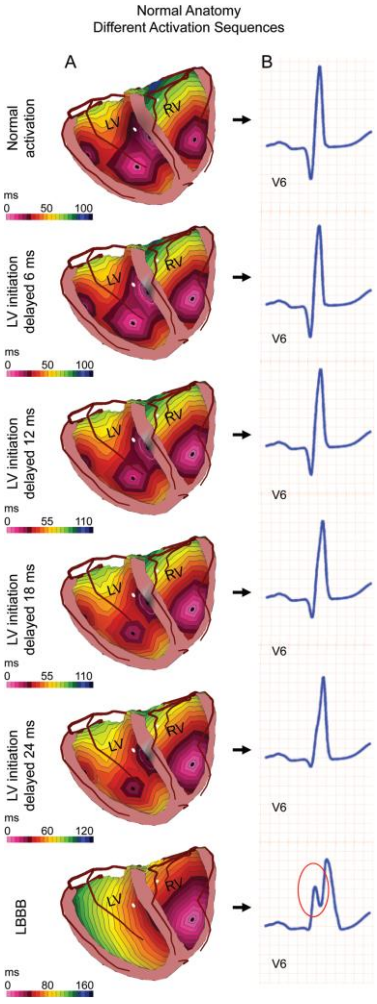
Paper 23

Lead author:	Galeotti, L	Year:	2013
Institution/s:	Radboud University Nijmegen, Food & Drug Administration		
Journal:	Europace		
Reference:	*Galeotti, L., van Dam, Peter M., Loring, Z., Chan, D., & Strauss, D.G. Evaluating Strict and Conventional Left Bundle Branch Block Criteria Using Electrocardiographic Simulations, Europace (2013). [Simulation]*		

Contribution to ECG Excellence technology:	Simulation of various conduction disorders using the ECGsim software

Abstract

Background Left bundle branch block (LBBB) is a critical predictor of patient benefit from cardiac resynchronization therapy (CRT), but recent studies suggest that one-third of patients diagnosed with LBBB by conventional electrocardiographic (ECG) criteria may have a false-positive diagnosis. In this study, we tested the hypothesis that recently proposed strict LBBB ECG criteria improve specificity in cases of left ventricular hypertrophy (LVH) /dilatation and incomplete LBBB.



Methods and results We developed five heart models based on a healthy male with increasing degrees of LV hypertrophy and/or dilation. With each model, we simulated six conduction types: normal conduction, four increments of delayed initiation of LV activation (incomplete LBBB), and complete LBBB. Simulated ECGs were evaluated for the presence of LBBB by conventional (LV conduction delay and QRSd ≥120 ms) and strict ECG criteria (LV conduction delay, QRSd 140 ms men or ≥130 ms women, and mid-QRS notching in at least two of the leads I, aVL, V1, V2, V5, and/or V6). Both conventional and strict LBBB criteria had 100% sensitivity. However, conventional criteria falsely diagnosed LBBB in cases with LVH + LV dilated 10 mm, LVH or LV dilated 10 mm combined with LV initiation ≥6 ms after the right ventricle (RV), and with LV dilated 5 mm combined with LV initiation ≥12 ms after RV (48% specificity). Strict LBBB criteria resulted in no false positives (100% specificity).

Conclusions New strict LBBB criteria increase the specificity of complete LBBB diagnosis in the presence of LV hypertrophy/dilatation and incomplete LBBB, which is critical for selecting CRT patients.

Paper 24

Lead author:	van Dam, P	Year:	2014
Institution/s:	Radboud University Nijmegen		
Journal:	Europace		
Reference:	*van Dam, P.M., Proniewska, K., Maugenest, A-M., van Mieghem, N-M., Maan, A-C., & de Jaegere, P.P.T. Electrocardiographic imaging-based recognition of possible induced bundle branch blocks during transcatheter aortic valve implantations. Europace. 2014 May 1, 2014;16(5):750-7.*		

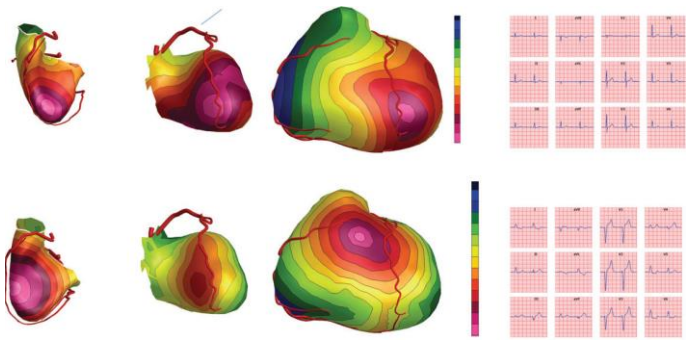
Contribution to ECG Excellence technology:	Tested the ability to map the conduction disorders that frequently occurred during trans catheter aortic valve implantation

Abstract:

Background: Conventional electrocardiogram (ECG)-based diagnosis of left bundle branch block (LBBB) in patients with left ventricular hypertrophy (LVH) is ambiguous. Left ventricular hypertrophy is often seen in patients with severe aortic stenosis in which a transcatheter aortic valve implantation (TAVI) frequently results in a LBBB due to the mechanical interaction of the artificial valve and the conduction system. In this feasibility study, we propose and evaluate the sensitivity of a new electrocardiographic imaging tool; the cardiac isochrone positioning system (CIPS), visualizing the cardiac activation to detect interventricular conduction patterns pre- and post-TAVI.

Methods and Results The CIPS translates standard 12-leadECGinto ventricular isochrones, representing the activation sequence. It requires a patient-specific model integrating heart, lungs, and other thoracic structures derived from multi-slice computed tomography. The fastest route-based algorithm was used to estimate the activation isochrones and the results were compared with standard ECG analysis. In 10 patients the CIPS was used to analyze 20 ECGs, 10 pre- and 10 post-TAVI. In 11 cases the CIPS results were in agreement with the ECG-based diagnosis. In two cases there was partial agreement and in seven cases there was disagreement. In four of these cases, the clinical history of the patients favored interpretation as assessed by CIPS, for the remaining three, it is unknown which method correctly classified the activation.

Conclusion This feasibility study applying the CIPS shows promising results to classify conduction disorders originating from the left anterior or posterior ventricular wall, or the septum. The visualization of the activation isochrones as well as ventricular model-derived features might support TAVI procedures and the therapy selection afterwards.



Paper 25

Lead author:	Coll-Font, J	Year:	2015
Institution/s:	NorthEastern University, Boston, USA		
Journal:	Computing in Cardiology Conference		
Reference:	*Coll-Font J, Erem B, Stovicek P, Brooks, D.H., van Dam, P.M. editors. Quantitative comparison of two cardiac electrical imaging methods to localize pacing sites. 2015 Computing in Cardiology Conference (CinC); 2015 6-9 Sept. 2015.*		

Contribution to ECG Excellence technology:	Localization of Pacing sites: Comparison of the used ECG Excellence technology technology with the potential layer source model (e..g. used by Cardio Insight)

Abstract:

Electrocardiographic imaging (ECGI) is a technology with great potential to support pre-procedure planning for ablation interventions. However, since the inverse problem it tries to solve is ill-posed, it requires regularization to stabilize the solutions. There have been multiple approaches to attain this objective with different regularization techniques that impose spatial or temporal behaviour on the solution based on prior electrophysiological knowledge with softer or harder constraints. It is continuing research to determine which prior knowledge added is better suited in each situation and there is a need to compare different methods on the same dataset to resolve that question. Here we compare two temporal methods that lie at both sides of the softness/hardness imposition of the prior knowledge. In one hand the splines method by Erem et al. imposes smoothness on the solution, while the cardiac isochrone positioning system (CIPS) forces the solutions to be step-function shaped in time. For this comparison we use the PSTOV dataset from the consortium on electrocardiographic imaging www.ecg-imaging. org which consists of body surface data during pacing at endocardial sites from subjects with healthy ventricles. The results show that on average CIPS performs better than the splines method, although there is too high a degree of variability within and across subjects and pacing locations to be able to predict which method performs better in an individual case.

Clinical studies

Localization of Ischemia

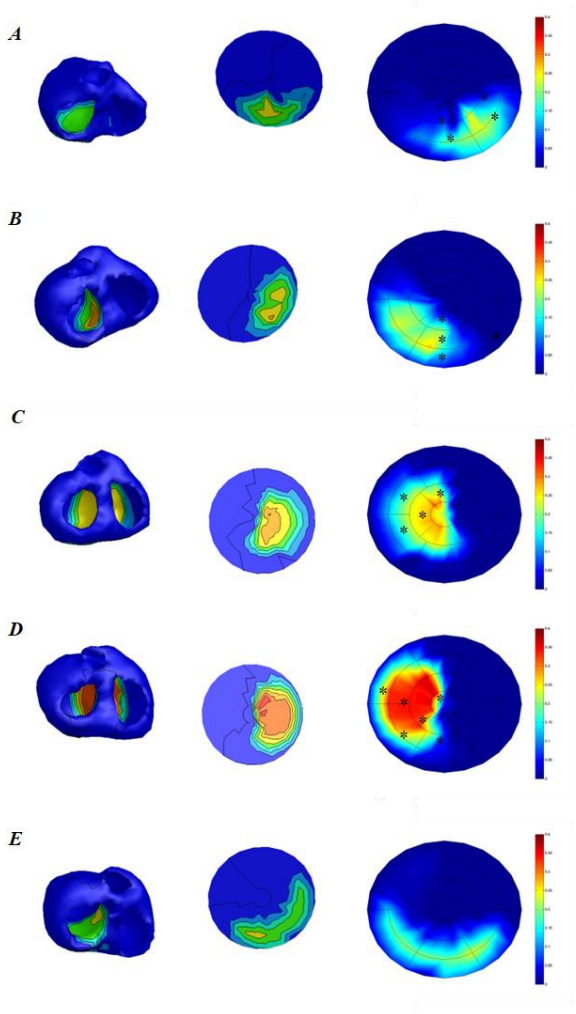
Paper 26

Lead author:	van Dam, P	**Year:**	2012
Institution/s:	Radboud University Nijmegen		
Journal:	IEEE Computer Society Press		
Reference:	*van Dam, P.M., Dijk, W.A., van der Putten, N.H.J., Maan, A.C., & de Jongste, M.J.J. Estimating Infarct Severity from the ECG using a Realistic Heart Model. Computing in Cardiology; 2012; Krakow, Poland: IEEE Computer Society Press*		

Contribution to ECG Excellence technology:	Modeling and understanding the localization and electrical tissue changes during infarction

Abstract:

The early phase of myocardial infarction is accompanied by changes in the ST segment of the ECG. This makes the ST segment the clinical marker for the detection of acute myocardial infarction. The determination of the infarct severity, location and size of the myocardial tissue at risk will support clinical decision making. In this study we used an inverse procedure to estimate the location and size of the infarcted heart region. The method estimates the local transmembrane amplitude based on the ECG amplitude near the J-point of the standard 12 leads signals using a patient specific volume conductor model. For the 5 available patient cases the positions as well as the size of the estimated infarct region were in accordance with results based on MRI.



ECGI: Technical Achievements to Clinical Applications

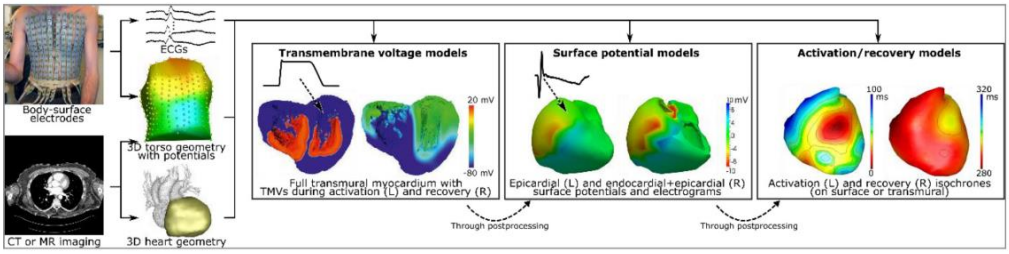
Paper 27

Lead author:	Cluitmans, M	**Year:**	2018
Institution/s:	Radboud University Nijmegen		
Journal:	Frontiers in Physiology		
Reference:	*Cluitmans, M., Brooks, D.H., MacLeod, R., Dössel, O., Guillem, M.S., van Dam, P.M., Svehlikova, J., He, B., Sapp, J., Wang, L., & Bear, L. Validation and Opportunities of Electrocardiographic Imaging: From Technical Achievements to Clinical Applications. Frontiers in Physiology. 2018;9(1305).*		

Contribution to ECG Excellence technology:	Overview of several iECG methods and their clinical application

Abstract:

Electrocardiographic imaging (ECGI) reconstructs the electrical activity of the heart from a dense array of body-surface electrocardiograms and a patient-specific heart-torso geometry. Depending on how it is formulated, ECGI allows the reconstruction of the activation and recovery sequence of the heart, the origin of premature beats or tachycardia, the anchors/hotspots of re-entrant arrhythmias and other electrophysiological quantities of interest. Importantly, these quantities are directly and non-invasively reconstructed in a digitized model of the patient's three-dimensional heart, which has led to clinical interest in ECGI's ability to personalize diagnosis and guide therapy. Despite considerable development over the last decades, validation of ECGI is challenging. Firstly, results depend considerably on implementation choices, which are necessary to deal with ECGI's ill-posed character. Secondly, it is challenging to obtain (invasive) ground truth data of high quality. In this review, we discuss the current status of ECGI validation as well as the major challenges remaining for complete adoption of ECGI in clinical practice. Specifically, showing clinical benefit is essential for the adoption of ECGI. Such benefit may lie in patient outcome improvement, workflow improvement, or cost reduction. Future studies should focus on these aspects to achieve broad adoption of ECGI, but only after the technical challenges have been solved for that specific application/pathology. We propose 'best' practices for technical validation and highlight collaborative efforts recently organized in this field. Continued interaction between engineers, basic scientists, and physicians remains essential to find a hybrid between technical achievements, pathological mechanisms insights, and clinical benefit, to evolve this powerful technique toward a useful role in clinical practice.



CineECG: The link between ECG and cardiac anatomy in Brugada patients

Paper 28

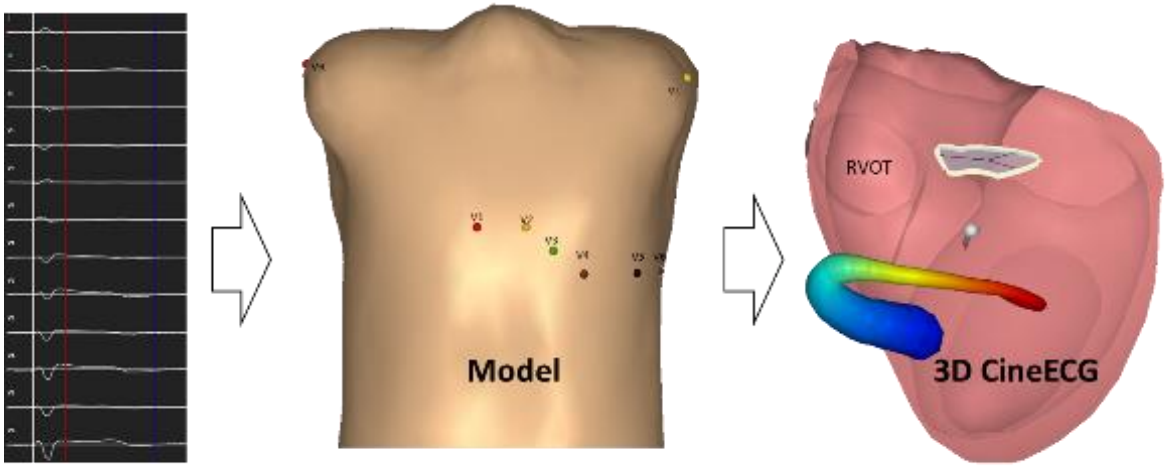
Lead author:	Peter van Dam	Year:	2020
Institution/s:	UMC Utrecht		
Journal:	Circulation A&E		
Reference:	*Dam PMv, Locati ET, Ciconte G, Borrelli V, Heilbron F, Santinelli V, Vicedomini G, Monasky MM, Micaglio E, Giannelli L, Mecarocci V, Ćalović Ž, Anastasia L and Pappone C. Novel CineECG Derived From Standard 12-Lead ECG Enables Right Ventricle Outflow Tract Localization of Electrical Substrate in Patients With Brugada Syndrome. Circulation: Arrhythmia and Electrophysiology. 2020;13:e008524.*		

Contribution to CineECG Development:	Application of the CineECG to the classification of Brugada patients

Abstract:

Background: In Brugada Syndrome (BrS), diagnosed in presence of a spontaneous or Ajmaline-induced type-1 pattern, ventricular arrhythmias originate from the right ventricle outflow tract (RVOT). We developed a novel CineECG method, obtained by inverse electrocardiogram (iECG) from standard 12-lead ECG, to localize the electrical activity pathway in BrS patients.

Methods: The CineECG enabled the temporo-spatial localization of the ECG waveforms, deriving the mean temporo-spatial isochrone (mTSI) from standard 12-lead ECG. The study sample included: a) 15 spontaneous BrS patients, and b) 18 Ajmaline-induced BrS patients (at baseline and after Ajmaline), in whom epicardial potential duration maps (PDM) were available; c) 17 type-3 BrS pattern patients not showing type-1 BrS pattern after Ajmaline (Ajmaline-negative); d) 47 normal subjects; e) 18 right bundle branch block (RBBB) patients.



According to CineECG algorithm, each ECG was classified as “Normal”, “Brugada”, “RBBB”, or “Undetermined”.

Results: In spontaneous or Ajmaline-induced BrS patients, CineECG localized the terminal mTSI forces in the RVOT, congruent with the arrhythmogenic substrate location detected by epicardial PDMs. The RVOT location was never observed in normal, RBBB, or Ajmaline-negative patients. In most Ajmaline-induced BrS patients (78%), the RVOT location was already evident at baseline. The CineECG classified all normal subjects and Ajmaline-negative patients at baseline as “Normal” or “Undetermined”, all RBBB patients as “RBBB”, while all spontaneous and Ajmaline-induced BrS patients as “Brugada”. Compared to standard 12-lead ECG, CineECG at baseline had a 100% positive predictive value and 81% negative predictive value in predicting Ajmaline-test results.

Conclusions: In spontaneous and Ajmaline-induced BrS patients, the CineECG localized the late QRS activity in the RVOT, a phenomenon never observed in normal, RBBB, or Ajmaline-negative patients. The possibility to identify the RVOT as the location of the arrhythmogenic substrate by the non-invasive CineECG, based on the standard 12-lead ECG, opens new prospective for diagnosing BrS patients.

CineECG in COVID patients

Paper 29

Lead author:	Peter M van Dam	Year:	2020
Institution/s:	UMC Utrecht		
Journal:	IEEE Computer Society Press		
Reference:	*PM van Dam, M. Boonstra, R Roudijk, MPM Linschoten, ET Locati, P Loh et al. The Electro-Anatomical Pathway for Normal and Abnormal ECGs in COVID Patients. Computing in Cardiology; 2020;Rimini, Italy:*		

Contribution to CineECG Development:	*The Electro-Anatomical Pathway for Normal and Abnormal ECGs in COVID Patients.*

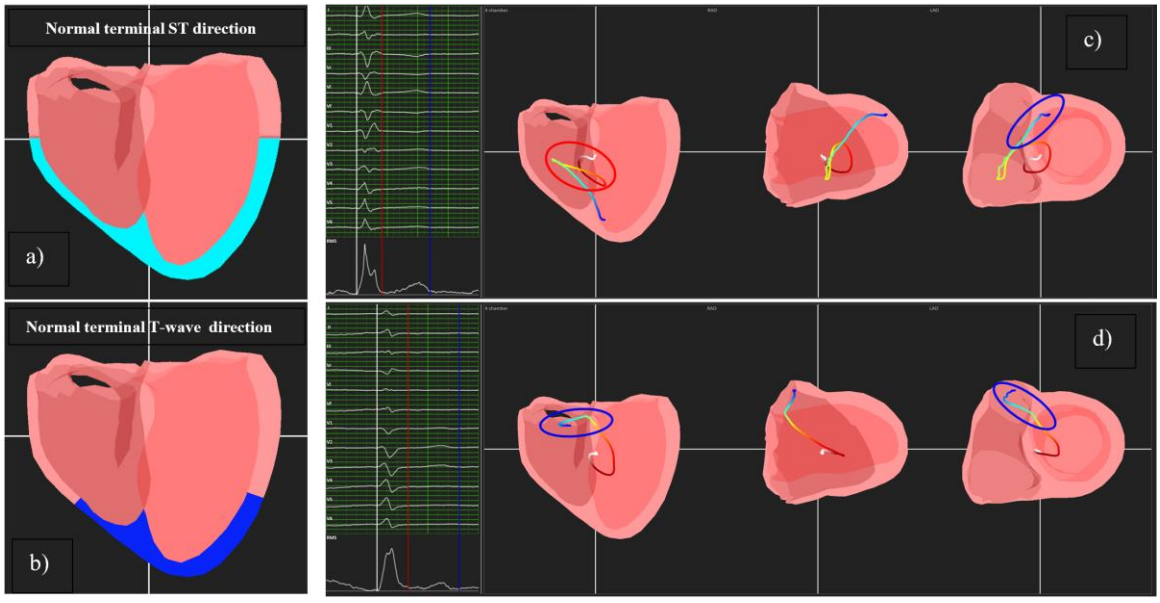
Abstract:

Patients with COVID-19 frequently have non-typical ECG changes in the QRS and T-wave morphology. The novel CineECG uses using the mean temporal spatial isochrones (mTSI) to relate the activation and recovery pathway to the cardiac anatomy. The aim of this feasibility study is to use the novel CineECG to separate normal from abnormal ECGs.

The ECGs of 100 normal controls were used to obtain the normal mTSI paths values for the QRS, ST segment and T-wave. These normal CineECG values were used to classify the COVID-19 ECGs as either as normal or abnormal of 107 patients being treated for COVID-19 in the University Medical Center Utrecht.

The CineECG was able to classify 98% of the normal ECG correctly and 94% of the abnormal ECG in comparison to expert ECG classifications.

The ability of the CineECG to relate the ECG to the cardiac anatomy supports the detection of abnormal ECGs. The CineECG might be a novel ECG screening tool to detect potential cardiac involvement of the COVID-19 disease for non-ECG experts.



CineECG localization and classification of conduction problems

Paper 30

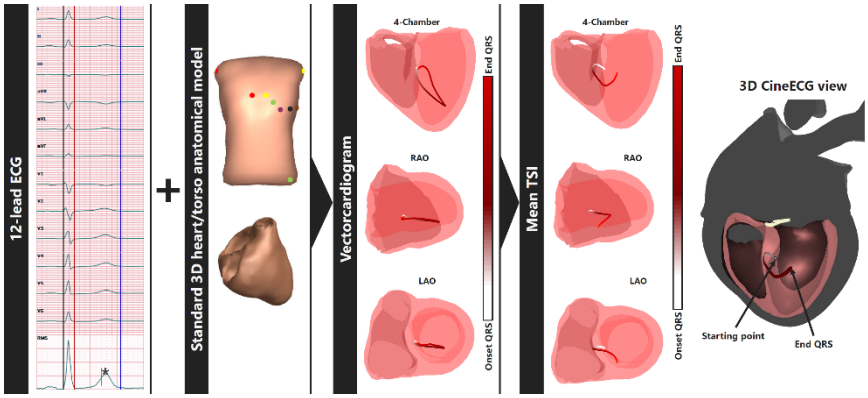
Lead author:	Boonstra, M	Year:	2021
Institution/s:	UMC Utrecht		
Journal:	EuroPace		
Reference:	*Boonstra MJ, Hilderink BN, Locati ET, Asselbergs FW, Loh P and van Dam PM. Novel CineECG enables anatomical 3D localization and classification of bundle branch blocks. EP Europace. 2021;23:i80-i87.*		

Contribution to CineECG Development:	Application of the CineECG to the classification of bundle branch blocks

Abstract:

Ventricular conduction disorders can induce arrhythmias and impair cardiac function. Bundle branch blocks (BBBs) are diagnosed by 12-lead electrocardiogram (ECG), but discrimination between BBBs and normal tracings can be challenging. CineECG computes the temporo-spatial trajectory of activation waveforms in a 3D heart model from 12-lead ECGs. Recently, in Brugada patients, CineECG has localized the terminal components of ventricular depolarization to right ventricle outflow tract (RVOT), coincident with arrhythmogenic substrate localization detected by epicardial electro-anatomical maps. This abnormality was not found in normal or right BBB (RBBB) patients. This study aimed at exploring whether CineECG can improve the discrimination between left BBB (LBBB)/RBBB, and incomplete RBBB (iRBBB).

Methods and results: We utilized 500 12-lead ECGs from the online Physionet-XL-PTB-Diagnostic ECG Database with a certified ECG diagnosis. The mean temporo-spatial isochrone trajectory was calculated and projected into the anatomical 3D heart model. We established five CineECG classes: 'Normal', 'iRBBB', 'RBBB', 'LBBB', and 'Undetermined', to which each tracing was allocated. We determined the accuracy of CineECG classification with the gold standard diagnosis. A total of 391 ECGs were analysed (9 ECGs were excluded for noise) and 240/266 were correctly classified as 'normal', 14/17 as 'iRBBB', 55/55 as 'RBBB', 51/51 as 'LBBB', and 31 as 'undetermined'. The terminal mean temporal spatial isochrone contained most information about the BBB localization.



Conclusion: CineECG provided the anatomical localization of different BBBs and accurately differentiated between normal, LBBB and RBBB, and iRBBB. CineECG may aid clinical diagnostic work-up, potentially contributing to the difficult discrimination between normal, iRBBB, and Brugada patients.

3D camera guided ECG electrode placement

Paper 31

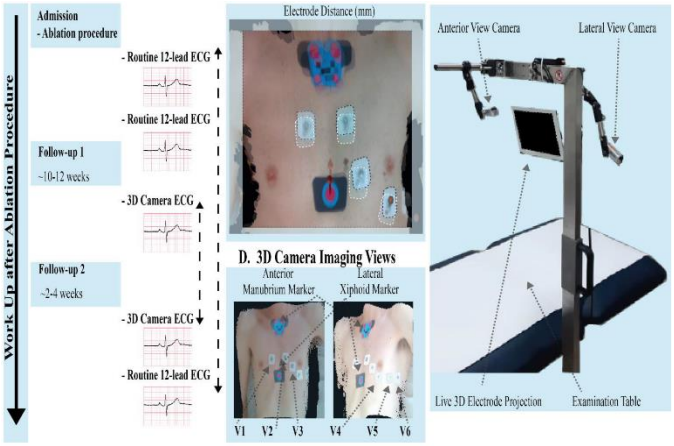
Lead author:	Roudijk, R	Year:	2021
Institution/s:	UMC Utrecht		
Journal:	Journal of Electrocardiography		
Reference:	*Robert W. Roudijk, Machteld J. Boonstra, Janna Ruisch, Martin Kastelein, Eelco van Dam, Menno Schellenkens, Peter Loh, Peter M. van Dam, Feasibility study of a 3D camera to reduce electrode repositioning errors during longitudinal ECG acquisition Vol. 66 Pages 69-76*		

Contribution to CineECG Development:	First clinical proof the 3D camera adds stability to the ECG recordings

Abstract:

Introduction: Longitudinal monitoring of sometimes subtle waveform changes of the 12-lead electrocardiogram (ECG) is complicated by patient-specific and technical factors, such as the inaccuracy of electrode repositioning. This feasibility study uses a 3D camera to reduce electrode repositioning errors, reduce ECG waveform variability and enable detailed longitudinal ECG monitoring.

Methods: Per subject, three clinical ECGs were obtained during routine clinical follow-up. Additionally, two ECGs were recorded guided by two 3D cameras, which were used to capture the precordial electrode locations and direct electrode repositioning. ECG waveforms and parameters were quantitatively compared between 3D camera guided ECGs and clinical ECGs. Euclidian distances between original and repositioned precordial electrodes from 3D guided ECGs were measured.



Results: Twenty subjects (mean age 65.1 ± 8.2 years, 35% females) were included. The ECG waveform variation between routine ECGs was significantly higher compared to 3D guided ECGs, for both the QRS complex (correlation coefficient = 0.90 vs 0.98, p<0.001) and the STT segment (correlation coefficient = 0.88 vs. 0.96, p<0.001). QTc interval variation was reduced for 3D camera guided ECGs compared to routine clinical ECGs (5.6 ms vs. 9.6 ms, p=0.030). The median distance between 3D guided repositioned electrodes was 10.0 [6.4–15.2] mm, and did differ between males and females (p=0.076).

Conclusions: 3D guided repositioning of precordial electrodes resulted in, a low repositioning error, higher agreement between waveforms of consecutive ECGs and a reduction of QTc variation. These findings suggest that longitudinal monitoring of disease progression using 12-lead ECG waveforms is feasible in clinical practice.

CineECG: Comparison to average activation sequence in the heart

Paper 32

Lead author:	Boonstra, M	Year:	2021
Institution/s:	UMC Utrecht		
Journal:	Computers in Biology and Medicine		
Reference:	*Machteld J. Boonstra, Dana H. Brooks, Peter Loh, Peter M. van Dam:* A novel method to image the average activation sequence in the heart from the 12-lead ECG. Computers in biology and medicine. 2021:105128.		

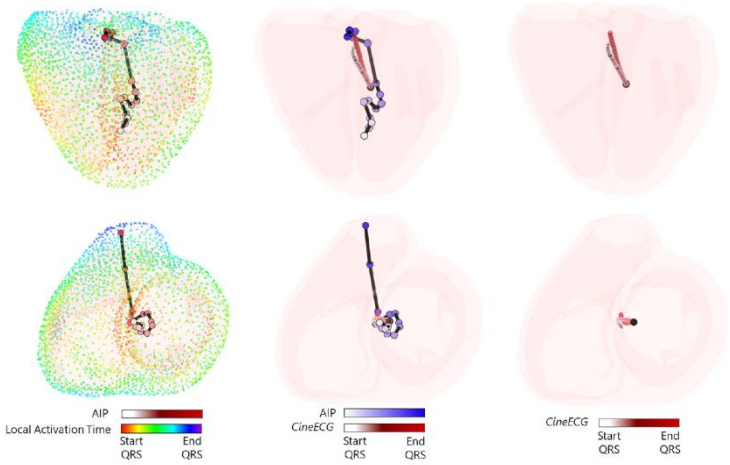
Contribution to CineECG Development:	Relationship between anatomical location of the isochrones and the CineECG position

Abstract:

Introduction: The standard 12-lead electrocardiogram (ECG) is a diagnostic tool to asses cardiac electrical activity. The vectorcardiogram is a related tool that represents that activity as the direction of a vector. In this work we investigate CineECG, a new 12-lead ECG based analysis method designed to directly estimate the average cardiac anatomical location of activation over time. We describe CineECG calculation and a novel comparison parameter, the average isochrone position (AIP).

Methods: In a model study, fourteen different activation sequences were simulated and corresponding 12-lead ECGs were computed. The CineECG was compared to AIP in terms of location and direction. In addition, 67-lead body surface potential maps from ten patients were used to study the sensitivity of CineECG to electrode mispositioning and anatomical model selection. Epicardial activation maps from four patients were used for further evaluation.

Results: The average distance between CineECG and AIP across the fourteen sequences was 23.7 ± 2.4 mm, with significantly better agreement in the terminal (27.3 ± 5.7 mm) versus the initial QRS segment (34.2 ± 6.1 mm). Up to four cm variation in electrode positioning produced an average distance of 6.5 ± 4.5 mm between CineECG trajectories, while substituting a generic heart/torso model for a patient-specific one produced an average difference of 6.1 ± 4.8 mm.



Conclusions: Dominant epicardial activation map features were recovered. Qualitatively, CineECG captured significant features of activation sequences and was robust to electrode misplacement. CineECG provides a realistic representation of the average cardiac activation in normal and diseased hearts. Especially the terminal segment of the CineECG might be useful to detect pathology.

The normal ventricular CineECG

Paper 33

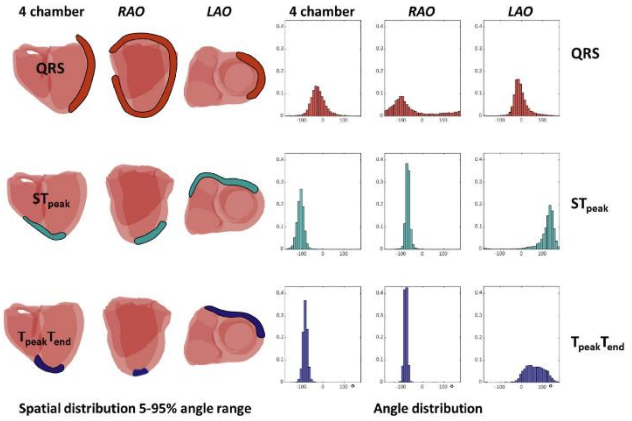
Lead author:	van Dam P.M.	Year:	2021
Institution/s:	UMC Utrecht		
Journal:	Journal of Electrocardiography		
Reference:	*van Dam PM, Boonstra M, Locati ET, Loh P. The relation of 12 lead ECG to the cardiac anatomy: The normal CineECG. Journal of Electrocardiology. 2021;69:67-74.*		

Contribution to CineECG Development:	The anatomical locations of the ventricular CineECG in normal males and females

Abstract:

Introduction: The interpretation of the 12-lead ECG is difficult and requires experts to distinguish normal from abnormal ECG waveforms. ECG waveforms depend on body build and electrode positions, both often different in males and females. To relate the ECG waveforms to cardiac anatomical structures is even more difficult. The novel CineECG enables a direct projection of the 12-lead ECG to the cardiac anatomy by computing the mean location of cardiac activity over time. The aim of this study is to investigate the cardiac locations of the CineECG derived from standard 12-lead ECGs of normal subjects.

Methods: In this study we used 6525 12-lead ECG tracings labelled as normal obtained from the certified Physionet PTB XL Diagnostic ECG Database to construct the CineECG. All 12 lead ECGs were analysed, and then divided by age groups (18–29,30-39,40-49,50-59,60-69,70–100 years) and by gender (male/female). For each ECG, we computed the CineECG within a generic 3D heart/torso model. Based on these CineECG's, the average normal cardiac location and direction for QRS, STpeak, and TpeakTend segments were determined.



Results: The CineECG direction for the QRS segment showed large variation towards the left free wall, whereas the STT segments were homogeneously directed towards the septal /apical region. The differences in the CineECG location for the QRS, STpeak, and peakTend between the age and gender groups were relatively small (maximally 10mmat end T-wave), although between the gender groups minor differences were found in the 4 chamber direction angles (QRS 4°, STpeak 5°, and TpeakTend 8°) and LAO (QRS 1°, STpeak 13°, and TpeakTend 30°).

Conclusions: CineECG demonstrated to be a feasible and pragmatic solution for ECG waveform interpretation, relating the ECG directly to the cardiac anatomy. The variations in depolarization and repolarization CineECG were small within this group of normal healthy controls, both in cardiac location aswell as in direction. CineECG may enable an easier discrimination between normal and abnormal QRS and T-wave morphologies, reducing the amount of expert training. Further studies are needed to prove whether novel CineECG can significantly contribute to the discrimination of normal versus abnormal ECG tracings.

The normal atrial CineECG

Paper 34

Lead author:	van Dam P.M.	Year:	2022
Institution/s:	UMC Utrecht		
Journal:	Journal of Electrocardiography		
Reference:	*Locati ET, Pappone C., Heilbron F., van Dam PM, CineECG provides a novel anatomical view on the normal atrial P-wave. European Hears journal: Digital Health. 2022.*		

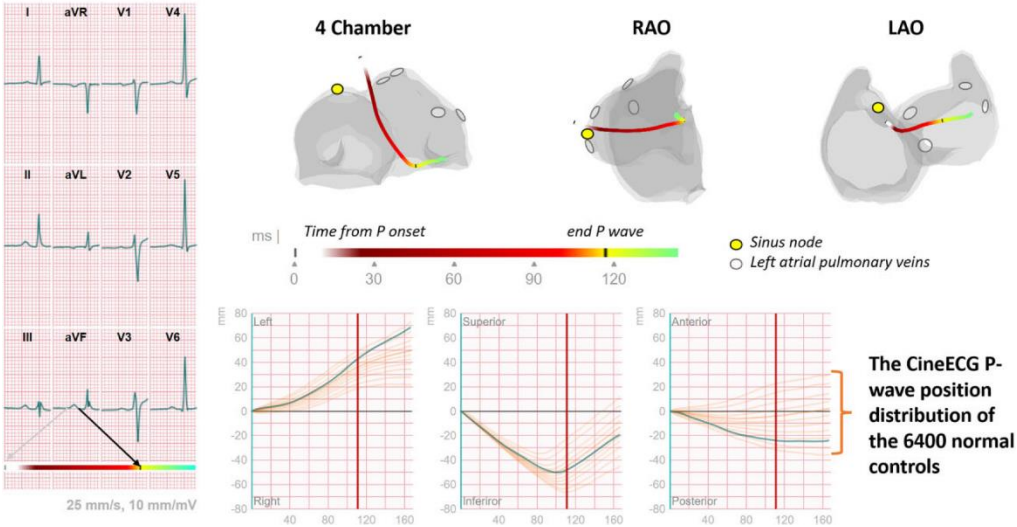
Contribution to CineECG Development:	The anatomical locations of the atrial CineECG in normal males and females

Abstract:

Introduction: Novel CineECG computed from standard 12-lead electrocardiogram (ECG) correlated the ventricular electric activity to ventricular anatomy. CineECG was never applied to reconstruct the spatial distribution of normal atrial electric activity into an atrial anatomic model.

Methods: From 6409 normal ECGs from PTB-XL database, we computed a median beat with fiducial points for P-and Q onset. To determine the temporo-spatial location of atrial activity during PQ-interval, CineECG was computed on a normal 58-year-old male atrial/torso model. CineECG was projected to three major cardiac axes: posterior anterior, right-left, base-roof, and to the standard cardiac four-chamber, left anterior oblique, and right anterior oblique (RAO) views.

sResults: In 6409 normal subjects, during P-wave, CineECG moved homogeneously from right atrial roof towards left atrial base (-54 ± 14 in four-chamber view, 95 ± 24 RAO view). During terminal PQ-interval, the CineECG direction was opposite, moving towards left atrial roof (62 ± 27in four-chamber view, 78 ± 27 RAO view). We identified the deflection point, where the atrial CineECG changes in direction. The time from P-onset to deflection point was similar to P-wave duration.



Conclusions: CineECG provided a novel three-dimensional visualization of atrial electrical activity during the PQ-interval, relating atrial electrical activity to the atrial anatomy. CineECG location during P-wave and terminal PQ-interval were homogeneous within normal controls. CineECG and its deflection point may enable the early detection of atrial conduction disorders predisposing to atrial arrhythmias.