Non-Invasive ECG Mapping To Guide Catheter Ablation

Ashok J. Shah, MD, Han S. Lim, MBBS, PhD, Seigo Yamashita, MD, Stephan Zellerhoff, MD, Benjamin Berte, MD, Saagar Mahida, MBChB, Darren Hooks, MD, Nora Aljefairi, MD, Nicolas Derval, MD, Arnaud Denis, MD, Frederic Sacher, MD, Pierre Jais, MD, Remi Dubois, PhD, Meleze Hocini, MD, Michel Haissaguerre, MD

Abstract
Since more than 100 years, 12-lead electrocardiography (ECG) is the standard-of-care tool, which involves measuring electrical potentials from limited sites on the body surface to diagnose cardiac disorder, its possible mechanism and the likely site of origin. Several decades of research has led to the development of a 252-lead-ECG and CT-scan based, three dimensional electro-imaging modality to non-invasively map abnormal cardiac rhythms including fibrillation. These maps provide guidance towards ablative therapy and thereby help advance the management of complex heart rhythm disorders. Here, we describe the clinical experience obtained using non-invasive technique in mapping the electrical disorder and guide the catheter ablation of atrial arrhythmias (premature atrial beat, atrial tachycardia, atrial fibrillation), ventricular arrhythmias (premature ventricular beats) and ventricular pre-excitation (Wolff-Parkinson-White syndrome).

Introduction
Since more than 100 years, 12-lead electrocardiography (ECG) is the standard-of-care tool which involves measuring electrical potentials from limited sites on the body surface to diagnose cardiac disorder, its possible mechanism and the likely site of origin. Several decades of research has led to the development of a 252-lead-ECG based three dimensional (3D) imaging modality to refine non-invasive diagnosis and improve the management of heart rhythm disorders. Here, we describe the clinical potential of this non-invasive mapping technique in identifying the sources of electrical disorders and guide the catheter ablation of atrial arrhythmias (premature atrial beat, atrial tachycardia, atrial fibrillation), ventricular arrhythmias (premature ventricular beats) and ventricular pre-excitation (Wolff-Parkinson-White syndrome).

Mapping Technique
The signal acquisition from the patient and subsequent computational methods used in the reconstruction of non-invasive maps using multiple torso electrodes have been previously described. Briefly, a 252-electrode vest is applied to the patient's torso and connected to the non-invasive imaging system and surface potentials are recorded. It is followed by a non-contrast thoracic CT scan to obtain high-resolution images of the heart and the vest electrodes. The 3D epicardial bicameral (atria or/and ventricles) geometries are reconstructed from segmental CT images. The relative positions of body surface electrodes can be visualized on the torso geometry. The system reconstructs epicardial potentials, unipolar electrograms, and activation maps from torso potentials during each beat/cycle using mathematical reconstruction algorithms. Details of the mathematical methods have been provided in detail elsewhere.

Atrial Arrhythmias
Atrial Fibrillation
In the area of atrial fibrillation (AF), noninvasive ECG mapping further contributes to our understanding of AF pathophysiology and facilitates catheter ablation. Currently, pulmonary vein (PV) isolation remains the cornerstone of catheter ablation for AF. Recently however, there is emerging evidence that AF may be driven and maintained by localized reentrant and focal sources in the atria. Mapping these localized sources proves to be difficult, as AF is essentially a dynamic rhythm. Previous mapping techniques utilizing single point catheters, regional multielectrode catheters, or surgical plaques have been restricted by several factors, such as the inability to map both atria simultaneously, catheter contact issues, and limited surgical access. With the advent of noninvasive mapping, AF may be mapped beat-to-beat in a panoramic fashion, allowing the identification of potential driving sources.

Non-Invasive Mapping Approach
Atrial cardiac potentials are much finer compared to ventricular potentials. To noninvasively map the atria accurately, several key barriers need to be overcome. As aforementioned, individual patient-specific 3-dimensional (3D) biatrial geometry is obtained from high-resolution noncontrast computed tomography (CT) scans undertaken with a 252 electrode vest applied to the patient's torso. The exact locations of body surface electrodes in relation to the cardiac geometry are obtained during the same CT scan. Consecutive windows with R-R pauses ≥1000ms during AF are analyzed. To avoid QRST interference, only the T-Q segments are

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None.

Corresponding Author:
Ashok J. Shah
Department of Rhythmologie
Service du Pr Haissaguerre
Hôpital Cardiologique du Haut-Lévêque
33604 Bordeaux-Pessac, France.
selected for analysis. In patients with rapid ventricular rates, diltiazem may be administered to slow atrioventricular (AV) conduction in order to create adequate recording windows.\(^{15}\) Filtering processes are applied to remove artifacts in signal morphology.\(^{12,14}\)

Activation maps are computed utilizing the intrinsic deflection-based method on unipolar electrograms (-dV/dTmax).\(^{14-16}\) With the global recording of cardiac signals, phase mapping algorithms may be applied to create AF maps, whereby a representation of the depolarization and repolarization wavefronts are computed from the isophase values corresponding respectively to π/2 and -π/2.\(^{15}\) Movies of wave propagation patterns are then displayed on the individualized biatrial geometry of each patient.

With the above technique, two general types of AF drivers have been identified: (1) reentrant, when a wave is observed to fully rotate around a functional core on phase progression; and (2) focal, when a wavefront originates from a focal site with centrifugal activation (Figure 1). Reentrant drivers are verified by sequential activation of local unipolar electrograms around a pivot point that covers the local cycle length, and focal drivers are confirmed by a QS pattern on unipolar electrograms. Due to the meandering nature of reentrant drivers observed in AF, the CT-based biatrial geometry is divided into regional domains for classification.\(^{15}\) An aggregated driver-density map is then created in each individual patient that summates all the drivers recorded in each window and is projected on the patient’s biatrial geometry.

**Paroxysmal AF**

In paroxysmal AF, noninvasive mapping successfully identifies focal drivers arising from the PVs.\(^{12,14}\) Centrifugal spread of the wavefront is demonstrated both by activation and phase mapping.\(^{12,14}\) The most remarkable finding is the observation of repetitive activation breakthroughs emanating from one or several PVs (simultaneously or sequentially) which generate reentrant drivers/rotor activity along the PV ostia. The validity of mapping is confirmed by termination of AF during isolation of the culprit PV.\(^{17,18}\) The mutual interplay between focal discharges from the PV and ensuing reentrant activity, therefore, confirms prior experimental observations made by Jalife et al and Chen et al on optical maps.\(^{17,18}\)

We mapped\(^{20}\) consecutive patients with clinical paroxysmal AF non-invasively to guide catheter ablation. The invasive procedure consisted of multispline mapping at sites of non-invasively identified sources and RF application at these target sites with the endpoint of AF termination. Non-invasive maps showed single or repetitive discharges from one or several pulmonary veins, coexisting with rotor drifting along the venous ostia in the posterior wall. The pulmonary vein discharges either extinguished or reset a pre-existing rotor. The

**Figure 1:** Phase mapping showing posterior view of left atrium during paroxysmal AF. Panel A shows serial snapshots of a single wave emerging out of the left inferior PV (white star) and reaching right veins in 30ms while it expands radially to the roof and inferior walls. Panel B shows serial snapshots of two successive rotations (white arrows) of a rotor located near the ostia of right veins. The core of the rotor (white star at the center of rainbow-coloured phases of rotor) is seen meandering in a small region in this example. The blue wave indicates the depolarizing front, which makes one full rotation in 160ms. The phases of wave propagation are color-coded using rainbow scale. The blue colour represents depolarizing wave and the green represents the end of repolarization. The wavefront can be read by following the blue colour. The time (ms) at the bottom of each snapshot represents the moment in the time-window when the snapshot was taken. Movie I in the online Data Supplement demonstrates these patterns with continuous non-invasive AF imaging. Abbreviations: LSPV: left superior pulmonary vein; LIPV: left inferior PV; RSPV: right superior PV; RIPV: right inferior PV, SVC: superior vena cava

“From Haissaguerre et al, Journal of Cardiovascular Electrophysiology 2013;24:711-7; with permission.”

**Figure 2:** Upper and Middle Panel: The endpoint of local ablation is increase in local cycle length and transformation of rapid and complex signals into simple and slower local rhythm. Lower Panel: It is not desirable to achieve complete electrogram abolition locally which results in tissue scarring post ablation.
In persistent AF, the identification of AF drivers helps pin point the targets for substrate ablation. A cohort of patients with paroxysmal and persistent AF, Cuculich et al. described diverse AF activation patterns that included multiple wavelets, rotors and focal sources with the use of noninvasive activation mapping.14

In the recent study by Haissaguerre et al.,15 103 consecutive patients undergoing catheter ablation for persistent AF were investigated using noninvasive phase mapping. A median of 4 driver regions was identified in patients with persistent AF. Of the recorded driver activity, 80.5% were reentrant and 19.5% were focal. Reentrant AF drivers were commonly located in the right PV/septal region, left PV/LA appendage region, left inferior wall/coronary sinus region and the superior right atrium; however, the exact locations varied amongst individuals.15 Reentrant activity was noted to be periodic, with the median number of continuous rotations being 2.6, but would often recur at the same or adjacent site. On the other hand, an average of 6 events was noted from a focal site.

In a subset of patients in this study, electrogram characteristics of AF driver versus non-driver regions were compared using an invasive multielectrode catheter. Regions harboring reentrant AF drivers more often demonstrated prolonged fractionated electrograms, and the recorded electrograms spanned across a large part of the AF cycle length. Studies are underway to delineate the electrogram characteristics of these reentrant activities. However, fractionation alone is non-specific, as it can be influenced by contiguous anatomical structures, slow or anisotropic conduction, and the direction or overlap of multiple wavefronts.20 A previous study however, has indicated that these reentrant drivers tended to harbor in the patchy zones bordering dense fibrotic areas.15,21,22

The aggregated driver-density map derived from noninvasive mapping serves as a roadmap for ablation. Point-by-point lesions are applied at the area harboring reentrant or focal drivers, starting with the region of highest driver-density and proceeding in a decreasing order. Local cycle length slowing is pursued as an endpoint of regional ablation, where initial electrograms are often rapid and fractionated. They are targeted until they become slower and less complex (figure 2) usually harboring synchronous activation on distal and proximal electrodes of the ablation catheter (indicative of passive activation). Figures 3 shows an example of an aggregated map to guide ablation of focal and reentrant drivers. In the ablation approach by Haissaguerre et al,15 following ablation of all driver regions, linear ablation was undertaken if AF persisted. Remapping during ablation procedure may identify the emergence of new drivers and thus may avoid linear ablation. All intermediate atrial tachycardias upon termination of AF were also subsequently ablated.

Using this approach, AF was acutely terminated in 80% of patients. The number of driver regions targeted to achieve AF termination...
in the non-invasive diagnosis of left atrial macroreentrant AT events. Of ectopic beats, making the approach impractical in intermittent systems, which necessitates sustained AT or repetitive occurrence of the diagnostic method employed by current invasive electroanatomic systems, requiring data from a wide range of patients using the non-invasive tool to define the mechanism of AT: macroreentrant (perimital, cavitricuspid isthmus-dependent and roof-dependent circuits) vs. centrifugal focal activation and 2) locate the source of arrhythmia in centrifugal ATs (Figure 8). Fifty-two patients (age: 61±11 years; 42 male, structural heart disease in 18) with clinical AT (mean cycle length 284±85ms) including those arising de novo, after catheter or surgical AF ablation (n=27) and post-atriotomy were included from three world centers. All patients were first mapped bedside non-invasively, followed by invasive mapping and ablation. The invasive operator was blinded to the non-invasive diagnosis. Invasive electrophysiological mapping was performed using conventional electrogram and 3D electroanatomical mapping system guidance. Non-invasive map was considered accurate when its diagnosis and increased with the duration of persistent AF; a single dominant region was identified in only 9% of patients (figure 4). Figure 5 shows a typical record form of ablation procedure and figure 6 shows an interesting correlation with conventional ECG of fibrillatory waves.

Among 90 patients who completed 12-month follow-up, 64% of patients were in stable sinus rhythm (SR), 22% in AT and 20% in AF. Importantly, the strategy of driver-based ablation guided by noninvasive mapping achieved similar 12-month clinical outcomes to the conventional stepwise approach, but with half the amount of ablation (28 vs. 65 minutes for AF termination). In this setting, persistent AF ablation guided by noninvasive mapping of localized drivers offers the ability to direct therapy to localized AF driver regions, and the potential to minimize the extent of ablation.

**Atrial Premature Complex and Atrial Tachycardia**

Wang et al. reported first successful use of the technique in the non-invasive diagnosis of the source of a clinical atrial tachycardia. ECG imaging accurately located the earliest site of atrial activation during focal AT in a patient that had previously undergone two pulmonary vein (PV) isolation procedures. The tachycardia was successfully terminated with radiofrequency ablation at 23 minutes. Below, the corresponding biatrial images show reentrant drivers on the left (number of rotations of the reentrant drivers are represented by digits on the map) and focal breakthroughs on the right.

**Figure 5:** In a 68-year-old male with persistent AF of 7 months, the AF-driver record-form notes septum, inferior left atrium, left and right appendages as ablation target sites in sequence from 1 to 4 after more than 28 seconds of AF was analysed. The number of rotors and focal breakthroughs, RF ablation time, appendage cycle lengths and the endpoint / outcome of ablation are tabulated for each target site. AF terminated to AT during ablation of 4th target site (right appendage). Total RF time to achieve AF termination is 23 minutes. Below, the corresponding biatrial images show reentrant drivers on the left (number of rotations of the reentrant drivers are represented by digits on the map) and focal breakthroughs on the right.

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**Figure 6:** In a 67-year-old male, 5-month-persistent AF with negative f waves in II, III, F appears as the driver region during AF with positive f waves in II, III, F.
deductive information may suffice with regard to ablation of target source is deduced by demonstrating simultaneous activation of both structure and therefore not included or displayed on the map, a septal direct mapping of the septum. Since the septum is not an epicardial substrate.

with promising initial results to improve the accuracy in low voltage amplitude which further complicated and challenged the diagnosis, some post ablation atria exhibited substantially lower-ECG P-wave cycle analysis. This can be addressed clinically by administration of cycle (unmasked by QRST complex) which is necessary for single ventricular conduction, precluding the selection of a full tachycardia mechanism in 4 out of 48 (8%) evaluable ATs was 2:1 atrio-

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Out of 48 evaluable clinical ATs, ATs were diagnosed in the EP laboratory as macroreentrant and 21 as centrifugal arrhythmias. All of them were successfully terminated by ablation resulting in sinus rhythm in 44 or another AT in 4. The overall diagnostic accuracy compared to invasive EP diagnosis, the gold standard, was 92% (100% in patients without any previous ablation and 83% in patients with previous AF ablation(s)). Non-invasive mapping was particularly useful and adept at accurately diagnosing centrifugal ATs (100% success rate including 11 (58%) patients with previous AF ablation). In this study, the primary reason of failure to diagnose the arrhythmia mechanism in 4 out of 48 (8%) evaluable ATs was 2:1 atrioventricular conduction, precluding the selection of a full tachycardia cycle (unmasked by QRST complex) which is necessary for single cycle analysis. This can be addressed clinically by administration of atrioventricular node blockers or simple pacing maneuvers during the invasive procedure to unmask multiple P waves. In addition, some post ablation atria exhibited substantially lower-ECG P-wave amplitude which further complicated and challenged the diagnosis, contributing to lower accuracy in post AF ablation ATs (83%). Noise reduction using a signal-averaging algorithm is being investigated with promising initial results to improve the accuracy in low voltage substrate.

A potential limitation of the system is its inability to provide direct mapping of the septum. Since the septum is not an epicardial structure and therefore not included or displayed on the map, a septal source is deduced by demonstrating simultaneous activation of both chambers from the inter-atrial groove. While precise localization on the septum may not be feasible for septal-source ATs, the deductive information may suffice with regard to ablation of target

in the region of interest. Although there is evidence for differential activation of the contiguous endo-epicardium in the atria (in at least some of its parts), the difference, at best, could be considered modest considering that the atrial tissue is much thinner in most parts than the ventricular myocardium.

Ventricular Arrhythmias

Ventricular Premature Complex And Ventricular Tachycardia

Premature ventricular complexes (PVCs) or outflow tract ventricular tachycardias (VTs) are commonly encountered in clinical practice. Localizing the origin of these arrhythmias can be challenging in cases that occur infrequently or last transiently (ie. few beats). In this scenario, noninvasive mapping may be particularly useful. The use of noninvasive mapping to localize PVCs has been validated by electrophysiological studies. Intini et al. used the electrocardiomapping technique for the first time in a clinical setting to guide diagnosis and therapy of a focal ventricular tachycardia (VT) in a young athlete. Isolated ventricular ectopic beats of an identical morphology to the sustained tachycardia were mapped prior to the invasive procedure and their origin was localized to the left ventricular (LV) apical diverticulum.

In a study by Jamil-Copley et al., patients wore a body vest consisting 252-surface electrodes for noninvasive localization of these ventricular arrhythmias. Patients were allowed to ambulate and the vest was applied up to 5 hours prior to the procedure to capture the culprit arrhythmia. Cardiac potentials, activation maps and voltage maps were derived from noninvasive mapping. Noninvasive mapping successfully identified the outflow tract ventricular tachycardia / PVC origin in 96% of cases, correctly sublocalizing to specific areas in the right or left outflow tract. Acute success was achieved in 100% of patients and medium success was achieved in 92% of patients.

In animal models, the cardiac activation sequences during single or multipoint pacing and VT are accurately depicted by noninvasive mapping. The origin of activation and image activation sequence of torsades de pointes can also be identified noninvasively. In humans, Wang et al. demonstrated that noninvasive mapping provided further information on the site of initiation, VT mechanism (focal or reentrant) and depth of VT origin (epicardial, mid-myocardial or endocardial). The study examined 26 ventricular arrhythmias in

Figure 8: Focal paroxysmal AT arising from the anterior wall of the right superior pulmonary venous ostium was mapped accurately with the ECG mapping system (isochronal map shown) and successfully ablated at the corresponding site seen on the fluoroscopic image. AT terminated after 9 seconds of radiofrequency application. Abbreviations: IVC-Inferior Vena Cava, SVC-Superior Vena Cava, RAA-Right Atrial Appendage, LAA-Left Atrial Appendage
25 patients (tachycardias (n=9), premature beats) prior to (n=19) and during (n=4) the invasive procedure. Noninvasive ECG imaging was in agreement with invasive EP study in 10 out of 11 RV sites (91%) and in 11 out of 12 LV sites (92%). For the two patients with discrepancies between invasive and noninvasive modalities, the discrepant locations were in proximity to each other. For the patient with right posteroseptal RV location, ECGI imaged the right posterolateral base as the location. This patient had undergone previous ablations of a right posteroseptal accessory pathway (12-lead ECG) which was successfully ablated at the same site (local electrogram shown). Also inserted is a virtual electrogram (QS morphology) from the site of earliest ventricular activation over the manifest pathway. Abbreviations: Ao-Aortic root, LAD-Left Anterior Descending artery, LAO-Left Anterior Oblique, MV-Mitral Valve, PA-Pulmonary Artery, TV-Tricuspid Valve.

Figure 9: Top: Biventricular Isopotential map (yellow colour denotes the earliest activation) during premature ventricular complex (12-Lead ECG). Inserted is an epicardial virtual electrogram (QS morphology) from the earliest site. The local intracardiac electrograms at the same site before the start of successful ablation are shown. Bottom: Biventricular Isopotential map (yellow colour denotes the earliest activation) during preexcitation from a right posteroseptal accessory pathway (12-lead ECG) which was successfully ablated at the same site (local electrogram shown). Also inserted is a virtual electrogram (QS morphology) from the site of earliest ventricular activation over the manifest pathway.

Conclusion:
Various atrial and ventricular arrhythmias including complex fibrillatory processes can be mapped non-invasively to guide catheter ablation. Accordingly, AF is driven and maintained by localized reentrant and focal sources, which are predominantly mapped and targeted by RF ablation in the PV antra and contiguous posterior left atrium in paroxysmal AF. Persistent AF in the early months is maintained by drivers clustered in a few biatrial regions, most of them being unstable reentries. Driver ablation results in comparable success rate with less RF duration. The pre- and per-procedural utility of the system in panoramic 3D mapping expresses its potential to reduce invasive procedural, fluoroscopic and ablation times.

References:


