CARDIOINSIGHT™
NONINVASIVE 3D MAPPING SYSTEM

CLINICAL EVIDENCE SUMMARY

April 2017
### SUPPORTING EVIDENCE

**RHYTHM** | **PUBLICATIONS** | **SYNOPSIS**
---|---|---
**AF** |  - Driver Domains in Persistent Atrial Fibrillation (Haissaguerre, et al)  
  - Complexity and Distribution of Drivers in Relation to Duration of Persistent Atrial Fibrillation (Lim, et al)  
  - Multicenter evaluation of noninvasive biatrial mapping for persistent atrial fibrillation ablation – the AFACART Study (Knecht, et al)  
  - Non-invasive Cardiac Mapping in Clinical Practice (Dubois, et al) |  - The longer a patient is in AF, the more complex the AF becomes\(^1\)  
  - “The complexity of AF drivers increases with prolonged AF duration.”\(^{12}\)  
  - System can help reduce invasive procedure time by “... performing an important task of identification of AF drivers.”\(^1\)  
  - “Noninvasive mapping of AF drivers may potentially simplify ablation approaches for persistent AF”\(^2\)  
  - “…driver-based ablation guided by non-invasive mapping achieved similar 12-month clinical outcomes to the conventional stepwise approach but with half the amount of ablation”\(^3\) |

  - Clinical Impact of a Novel 3D Electrocardiographic Imaging for Non-invasive Mapping of Ventricular Arrhythmias (Erkapic, et al)  
  - Noninvasive electrocardiomapping Facilitates Previously Failed Ablation of Right Appendage Diverticulum Associated Life-Threatening Accessory Pathway (Hocini, et al) |  - “The system can accurately identify OTVT/PVC origin in the left and the right ventricle ... to guide catheter ablation with an accuracy superior to published ECG algorithms”\(^4\)  
  - System offers a “… useful tool to map VAs with high accuracy...”\(^5\)  
  - “Combination of structural (CT-scan) and functional (3D electrocardiomapping) imaging methods helped successfully accomplish ablation ... with a complex right atrial anomaly after previous unsuccessful attempts of endo-epicardial ablation guided by the invasive electroanatomic system in an adolescent female.”\(^8\)
## SUPPORTING EVIDENCE

<table>
<thead>
<tr>
<th>BENEFIT</th>
<th>PUBLICATIONS</th>
<th>SYNOPSIS</th>
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<tbody>
<tr>
<td>NON-INVASIVE</td>
<td>• Utility of Noninvasive Arrhythmia Mapping in Patients with Adult Congenital Heart Disease (Ernst, et al)&lt;br&gt;• Driver Domains in Persistent Atrial Fibrillation (Haissaiguerre, et al)&lt;br&gt;• Focal Arrhythmia Ablation Determined by High-Resolution Noninvasive Maps (Hocini, et al)&lt;br&gt;• Clinical impact of a novel 3D electrocardiographic imaging for non-invasive mapping of ventricular arrhythmias (Erkapic, et al)</td>
<td>• All studies demonstrated that pre-procedural mapping allowed for customization of ablation strategy by the physician&lt;sup&gt;1,5,9,10&lt;/sup&gt;&lt;br&gt;• One study observed reduction in procedural and/or ablation time&lt;sup&gt;5&lt;/sup&gt;&lt;br&gt;• Enables prolonged bedside monitoring which allows more physiologic conditions and transient events to be observed</td>
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<tr>
<td>MULTI-CHAMBER</td>
<td>• Driver Domains in Persistent Atrial Fibrillation (Haissaiguerre, et al)&lt;br&gt;• Multicenter evaluation of noninvasive biatrial mapping for persistent atrial fibrillation ablation – the AFACART Study (Knecht, et al)</td>
<td>• Simultaneous mapping of AF provides view of both atria at the same time&lt;sup&gt;1&lt;/sup&gt;&lt;br&gt;• The site of AF termination was the right atrium in 28% of cases&lt;sup&gt;2&lt;/sup&gt;&lt;br&gt;• Each patient had a different pattern of “drivers”&lt;sup&gt;1&lt;/sup&gt;</td>
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<tr>
<td>SINGLE BEAT</td>
<td>• Validation of Novel 3D electrocardiographic mapping of atrial tachycardias (Shah, et al)&lt;br&gt;• Clinical Experience Kerckhoff Klinik, Bad Nauheim, Germany&lt;br&gt;• Clinical impact of a novel 3D electrocardiographic imaging for non-invasive mapping of ventricular arrhythmias (Erkapic, et al)</td>
<td>• Simultaneous mapping allows one to identify electrical activity by chamber and region of interest&lt;sup&gt;5,6,11&lt;/sup&gt;&lt;br&gt;• “System identified the chamber of origin of the arrhythmia accurately in all cases (versus ECG accuracy of 76.5%). The site of origin was identified accurately in 97% of the cases (versus ECG accuracy of 26.5%).”&lt;sup&gt;11&lt;/sup&gt;</td>
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</table>
STUDIES OF AF
Aims
Evaluate use of non-invasive 3D Mapping (ECM) to identify “drivers” in distinct categories of persistent atrial fibrillation (AF).

Methods
- Prospective, non-randomized
- RF Ablation times compared to matched controls
- n=103
- “Driver ablation” + PVI; + linear lesions if AF not terminated

Results
Acute results: 82/103 patients experienced AF termination (80%).

Average RF duration to terminate AF
Non-invasive mapping: 28 +/- 17 min.
Matched controls: 65 +/- 33 min.

Outcomes:
90/103 attained 12 month follow-up
58/90 (64%) in stable sinus rhythm at 12 mos
16/90 repeat ablations for atrial tachycardia (12) or AF (4)
85% with AF termination (60/71) free from AF at 12 mos, similar to matched controls (71/82)

Study Author’s Conclusion
“The noninvasive system can map AF pre-procedurally and help shorten invasive procedural time by performing an important task of identification of AF drivers.”

COMPLEXITY AND DISTRIBUTION OF DRIVERS IN RELATION TO DURATION OF PERSISTENT ATRIAL FIBRILLATION

Aims
“...to investigate the complexity and distribution of AF drivers in” Persistent AF (PeAF) of varying durations

Methods
- Prospective, non-randomized
- n=105 PeAF patients undergoing first AF ablation
  - PeAF presenting in SR = 32 pts
  - PeAF <12 months = 45 pts
  - PeAF >12 months = 28 pts

Results
- Pulmonary vein (PV) regions and inferoposterior left atrial wall were most prominent driver regions
- Focal drivers observed in 1 or both PV regions in 75% of patients
- AF complexity increased with increasing AF duration as shown by increased number of:
  - Re-entrant rotations (p < 0.05)
  - Re-entrant rotations and focal events (p < 0.05)
  - Regions harboring re-entrant (p < 0.01) and focal (p < 0.05) drivers
- Procedural AF termination was achieved in 70% of patients, but decreased with longer AF duration

Study Authors’ Conclusion
“The complexity of AF drivers increases with prolonged AF duration. ... AF termination rate declines as patients progress to longstanding persistent AF, underscoring the importance of early intervention.”
MULTICENTER EVALUATION OF NONINVASIVE BIATRIAL MAPPING FOR PERSISTENT ATRIAL FIBRILLATION ABLATION – THE AFACART STUDY

Aims
To evaluate the utility of ECG mapping as a practical tool prior to ablation for persistent AF in centers with no practical experience of the system

Methods
- Multicenter (8 centers), prospective, non-randomized
- N=118, PeAF <1 year, refractory to >1 AAD, LA diameter <55mm
- Primary endpoint: Acute AF to SR or AT
  - 3 month blanking period (Failure =AF or AT > 30secs)
  - Holters at 3, 6*, 9, & 12* months (*=72 hours)
  - ATs were not ablated

Results
- Driver-only ablation resulted in AF termination in 64% of the patients (75/118)
- Acute termination rates were not significantly different across all 10 centers.
- At 1 year, 77% of patients were free from AF recurrence after only a single procedure (78% off AADs)
- 14/25 recurrences were persistent of which 4 could not be managed by DC cardioversion ± new AADs ± repeat ablation

Results Cont.
- Remaining 11 AF recurrences were paroxysmal
- 37% of all patients developed atrial tachycardia managed by AAD ± repeat ablation

Study Authors’ Conclusion
“This multicentre study demonstrates that reproducible acute and chronic outcomes can be achieved by centres with no practical experience of the mapping system. … Targeting drivers identified by the system results in high rate of AF termination...”

NON-INVASIVE CARDIAC MAPPING IN CLINICAL PRACTICE: APPLICATION TO THE ABLATION OF CARDIAC ARRHYTHMIAS

Aims
Description of clinical experience in using non-invasive mapping technique to identify the sources of electrical disorders and guide catheter ablation of atrial and ventricular arrhythmias.

Methods/Background
- Prospective, non-randomized
- Patients mapped non-invasively:
  - 23 Paroxysmal AF
  - 103 Persistent AF
  - 52 with various clinical ATs
- Using the “driver-density map” as a guide, point-by-point lesions applied at area of reentrant or focal “drivers” of PeAF, “starting with region of highest driver density and proceeding in decreasing order.”

Results
- PAF: 657 “drivers” mapped; termination achieved in all
- PeAF: Acute termination = 80%; “driver-based ablation guided by non-invasive mapping achieved similar 12-month clinical outcomes to traditional approach but with half the amount of ablation”
- AT: all 48 evaluable clinical ATs were successfully terminated by ablation

Study Authors’ Conclusion
“Various atrial and ventricular arrhythmias including complex fibrillatory processes can be mapped non-invasively to guide catheter ablation. The pre- and peri-procedural utility of the system in panoramic 3D mapping expresses its potential to reduce invasive procedural, fluoroscopic and ablation times.”


Upper & Middle Panels: The endpoint of local ablation is increase in local cycle length and transformation of rapid and complex signals into slower local rhythm.

Lower Panel: It is not desirable to achieve complete electrogram abolition locally which results in tissue scarring post-ablation.
STUDIES OF VT
NON-INVASIVE ELECTROCARDIOGRAPHIC MAPPING TO GUIDE ABLATION OF OUTFLOW TRACT VENTRICULAR ARRHYTHMIAS

Aims
Assess the performance of non-invasive mapping (ECM) in the pre-/periprocedural localization of OTVT origin to guide ablation and to compare the accuracy of ECM with that of published pre-procedure ECG algorithms.

Methods
 Prospective, non-randomized
 n=24
 Noninvasive ECM (CIT) vs. pre-procedure ECG algorithms.

Results
Noninvasive ECM:
Chamber of origin identified 96%,
Sublocalizing correctly 100%.
Acute ablation success 100%.

Validated pre-procedure ECG Algorithms:
Chamber of origin identified 50–88%*
Sublocalizing 37–58%
(*results varied based on which of 3 algorithms used.)

Study Authors’ Conclusion
“ECM can accurately identify OTVT/PVC origin in the left and the right ventricle pre- and periprocedurally to guide catheter ablation with an accuracy superior to that of published ECG algorithms.”
Aims
Evaluate use of non-invasive 3D Mapping (ECM) in routine clinical mapping and ablation of ventricular arrhythmias (VAs)

Methods
- Prospective, randomized CardioInsight vs 12 lead ECG
- PVC with or without monomorphic VT
- n=42

Results

<table>
<thead>
<tr>
<th></th>
<th>CardioInsight</th>
<th>12 Lead ECG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chamber</td>
<td>20/21 (95.2%)</td>
<td>16/21 (76.2%)</td>
</tr>
<tr>
<td>Region of interest*</td>
<td>20/21 (95.2%)</td>
<td>8/21 (38.1%)</td>
</tr>
<tr>
<td># ablation*</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Procedure time*</td>
<td>78</td>
<td>89</td>
</tr>
<tr>
<td>Radiation exposure*</td>
<td>3.21 mSv</td>
<td>0.39 mSv</td>
</tr>
</tbody>
</table>

* = P-value ≤ 0.05

Outcomes: 3 month success rate
- CardioInsight (95.2%)
- ECG (100%)

Study Authors’ Conclusion
CardioInsight technology “…offers a clinically useful tool to map VAs with high accuracy and more targeted ablations superior to the body surface ECG but had significantly higher radiation exposure due to computer tomography scan.”

NONINVASIVE ELECTROCARDIOMAPPING FACILITATES PREVIOUSLY FAILED ABLATION OF RIGHT APPENDAGE DIVERTICULUM ASSOCIATED LIFE-THREATENING ACCESSORY PATHWAY

Aims
Case Study overview of successful ablation of accessory pathway with complex anatomy after previous unsuccessful attempts

Methods/Background
- Case study
- 14 year old girl presented with 8 year long history of palpitations

1. Failed EP study evaluation and ablation
   - EP study → AF → VF → DC
   - Several endocardial ablation attempts → FAILED ablation

2. Referred to Bordeaux; Failed EP study evaluation and ablation
   - EP study → AF → VF → DC
   - Endo-Epicardial ablation → Failed Ablation

3. ECVUE was used prior to surgical intervention
   - CT (with contrast) indicated giant right appendage and small diverticulum arising from lower end enveloping basal part of anterior right ventricle.
   - Activation maps from ECVUE demonstrated earliest activation located in basal right ventricle at site of collar connecting the appendage with diverticulum
   - Electrogram based mapping revealed earliest ventricular activation at site indicated by ECVUE

Results
Successful ablation with one single RF application led to permanent disappearance of pre-excitation

Symptom and Arrhythmia free off AADs after 5 months of successful procedure.

Study Conclusion
ECVUE system provided maps that the physician analyzed in order to create a successful ablation strategy after previous unsuccessful attempting of endocardial ablation.

Aims
Prospective evaluation of the role of a 3D non-invasive mapping system (ECM), in facilitating the diagnosis of atrial tachycardias (AT).

Methods
- Multicenter, Prospective, non-randomized
- 3 centers, n=52
- ECM with CIT compared to intracardiac 3D Mapping with Carto™*/Ensite for patients with Atrial Tachycardia

Results
ECM and EP Diagnosis achieved in 48/52 pts (92%)
In 4 patients clinical AT converted to another rhythm (AT, AF, or sinus) before invasive mapping could be completed therefore pts excluded from analysis.

ECM correctly diagnosed AT mechanisms in 44/48 (92%)
The 2:1 ventricular conduction and low-amplitude P waves challenged the diagnosis of 4/27 macroreentrant ATs that could be overcome by injecting AV node blockers and signal averaging, respectively.

Study Authors’ Conclusion
“This prospective multicenter series shows high success rate of ECM in accurately diagnosing the mechanism of AT and the location of focal arrhythmia.”
FOCAL ARRHYTHMIA ABLATION DETERMINED BY HIGH-RESOLUTION NONINVASIVE MAPS: MULTICENTER FEASIBILITY STUDY

Aims
Prospective evaluation of the role of a high resolution non-invasive mapping system for patients with PVC’s, AT’s, and WPW.

Methods
- Multicenter, Prospective, non-randomized
- 3 centers, n=33

Results
Successful ablation in 32/33 patients (97%) without complications.

Procedure Metrics
- Average time from catheterization to arrhythmia termination: 16 min
- Average RF Ablation time: 3.98 min
- Average Procedure time (skin-to-skin): 71 min
- Average Fluro time: 11.9 min

Average cumulative radiation exposure (CT scan and fluro): 7.57 mSv

<table>
<thead>
<tr>
<th>PROCEDURE DATA</th>
<th>MEAN ± SER</th>
<th>RANGE (MIN-MAX)</th>
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<tbody>
<tr>
<td>Atrial Tachycardia</td>
<td></td>
<td></td>
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<tr>
<td>Procedure time (minutes)</td>
<td>48.0 ± 24.0</td>
<td>(24-72)</td>
</tr>
<tr>
<td>Mapping time (minutes)</td>
<td>4.5 ± 0.6</td>
<td>(4.1-4.9)</td>
</tr>
<tr>
<td>Total RF (seconds)</td>
<td>387.5 ± 237.5</td>
<td>(150-625)</td>
</tr>
<tr>
<td>Fluoro time (minutes)</td>
<td>8.8 ± 1.5</td>
<td>(8-9)</td>
</tr>
<tr>
<td>RF to arrhythmia elimination (seconds)</td>
<td>8.5 ± 0.5</td>
<td>(8.0-46)</td>
</tr>
<tr>
<td>Wolff Parkinson White</td>
<td></td>
<td></td>
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<tr>
<td>Procedure time (minutes)</td>
<td>85.0 ± 15.1</td>
<td>(40-125)</td>
</tr>
<tr>
<td>Mapping time (minutes)</td>
<td>7.3 ± 2.2</td>
<td>(2.7-15.4)</td>
</tr>
<tr>
<td>Total RF (seconds)</td>
<td>717.0 ± 391.8</td>
<td>(96-2123)</td>
</tr>
<tr>
<td>Fluoro time (minutes)</td>
<td>12.9 ± 3.9</td>
<td>(4.76-25.98)</td>
</tr>
<tr>
<td>RF to arrhythmia elimination (seconds)</td>
<td>7.0 ± 1.7</td>
<td>(2.0-11)</td>
</tr>
<tr>
<td>Premature Ventricular Contraction</td>
<td></td>
<td></td>
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<tr>
<td>Procedure time (minutes)</td>
<td>76.7 ± 9.1</td>
<td>(11-222)</td>
</tr>
<tr>
<td>Mapping time (minutes)</td>
<td>15.0 ± 3.1</td>
<td>(5.0-68)</td>
</tr>
<tr>
<td>Total RF (seconds)</td>
<td>376.0 ± 70.0</td>
<td>(52-1654)</td>
</tr>
<tr>
<td>Fluoro time (minutes)</td>
<td>15.6 ± 2.6</td>
<td>(3.1-54.95)</td>
</tr>
<tr>
<td>RF to arrhythmia elimination (seconds)</td>
<td>26.1 ± 4.0</td>
<td>(2.0-72)</td>
</tr>
</tbody>
</table>

Study Authors’ Conclusion
CardioInsight system “... is a noninvasive tool allowing pre-procedural localization of the origin of the arrhythmia and direct RF delivery to the focal source without the need for intracardiac mapping.”
Aims
To provide a real world example of clinical experience to compare identification of chamber and site of origin of the arrhythmia in each patient using the mapping system and 12 lead ECG.

- N=29 underwent 12 lead ECG, non-invasive ECVUE mapping followed by an EP mapping procedure.
- Retrospective analysis of medical records of each patient documented by the attending physician for both mapping system and ECG.

Findings

### Percent agreement of CardioInsight System (N=29 cases)

<table>
<thead>
<tr>
<th></th>
<th>ECVUE</th>
<th>ECG (Standard of Care)</th>
</tr>
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<tbody>
<tr>
<td>Chamber</td>
<td>100%</td>
<td>76.5%</td>
</tr>
<tr>
<td>Site of Origin</td>
<td>97.1%</td>
<td>26.5%</td>
</tr>
</tbody>
</table>

Mapping system identified the chamber of origin of the arrhythmia accurately in all cases (versus ECG accuracy of 76.5%). The site of origin was identified accurately in 97% of the cases (versus ECG accuracy of 26.5%).

Findings cont.
Clinical complexity of these cases reviewed did not impact the ability to accurately identify chamber and site of origin using the mapping system, as supported by the 100% accuracy in patients with structural heart disease and patients who have undergone previous ablation procedures.

Source: Clinical Experience excerpt from ECVUE 510(k) final version Feb 26 2014
THANK YOU
INDICATION FOR USE

The CardiolInsight™ Noninvasive 3D Mapping System is intended for acquisition, analysis, display and storage of cardiac electrophysiological data and maps for analysis by a physician.

Indications, warnings and instructions for use can be found in the product labeling supplied with each device.

CAUTION: Federal (USA) law restricts these devices for sale by or on the order of a physician. This system is intended for use only by persons trained and/or under the guidance of Medtronic personnel (such as Field Clinical Engineers) as referenced in the system User Manual. The clinical significance of solely utilizing phase maps to classify arrhythmia mechanisms has not been extensively validated by clinical investigations.

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CITATIONS

11. Clinical Experience, Kerckhoff Klinik, Bad Nauheim, Germany. Part of 510k FDA submission for clearance.