Substrate and Electrogram Guided AF Ablation using High-Density Mapping

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Ablation Strategies for Persistent AF

- PV Antral Isolation only
- PVI + Non-PV triggers
- PVI + Linear lesions
- PVI + Post wall isolation
- EGM (CFAE) based ablation
- PVI + EGM based ablation
- PVI + Substrate based ablation
- Ablation of rotational activity
- ....
STAR AF II Trial

**Figure 2. Freedom from Atrial Fibrillation.**
The graph shows Kaplan-Meier estimates of freedom from documented atrial fibrillation more than 30 seconds after a single procedure, with or without the use of antiarrhythmic medications. There were no significant differences between groups (P=0.15). Isolation plus electrograms denotes ablation with pulmonary-vein isolation plus additional ablation of complex fractionated electrograms; isolation plus lines refers to ablation with pulmonary-vein isolation plus additional linear ablation.
AF Ablation Strategy: Expert Consensus

- **Posterior wall isolation might be considered** for initial or repeat ablation of persistent or long-standing persistent AF. (*Class IIb, LOE C-LD*)

- Administration of high-dose isoproterenol to screen for and then ablate **non-PV triggers may be considered** during initial or repeat AF ablation procedures in patients with paroxysmal, persistent, or long-standing persistent AF. (*Class IIb, LOE C-LD*)

- The usefulness of **linear ablation lesions** in the absence of macroreentrant atrial flutter is **not well established**. (*Class IIb, LOE C-LD*)

*Calkins H et al., Heart Rhythm. 2017;14:e275-e444.*
AF Ablation Strategy: Expert Consensus

- The usefulness of mapping and ablation of areas of abnormal myocardial tissue identified with voltage mapping or MRI as an initial or repeat ablation strategy for persistent or long-standing persistent AF is not well established. (Class IIb, LOE B-R)

- The usefulness of ablation of complex fractionated atrial electrograms as an initial or repeat ablation strategy for persistent and long-standing persistent AF is not well established. (Class IIb, LOE B-R)
Fibrosis and Atrial Fibrillation

Fibrotic Remodeling

- Increased Total Atrial Fibrosis
- Increased Patchy and Diffuse Fibrosis
- Increased Insulating Interstitial Fibrosis

Arrhythmogenic Conduction Disturbances

- Slow Conduction
- Unidirectional Block
- Intramural Block between Epicardial and Endocardial Myocardium
- Transverse Block between Myobundles

Microanatomic Reentry due to Fibrotic Insulation

Association of Atrial Fibrosis and AF Ablation

Figure 2. Four Stages of Left Atrial Tissue Fibrosis Based on 3D Delayed Enhancement Magnetic Resonance Imaging Scans

A Stage 1 (<10% of atrial wall)
B Stage 2 (10% - 20% of atrial wall)
C Stage 3 (20% - 30% of atrial wall)
D Stage 4 (>30% of atrial wall)

Representative example from 4 different patients of each stage of left atrial tissue fibrosis. Normal left atrial wall is displayed in blue; fibrotic changes are in green and white. Stages 1 through 4 show increasing amounts of fibrosis as a percentage of the total left atrial wall volume. The pulmonary veins and mitral valve are shown in gray.

Figure 4. Cumulative Incidence of Arrhythmia Recurrence Without Covariate Adjustment Through Day 475 After the Blanking Period

No. at risk
Stage 4 24 15 11 10 7 6
Stage 3 80 56 47 41 19 12
Stage 2 107 79 74 58 26 15
Stage 1 49 47 43 33 13 4

Small vertical ticks on curves indicate where a patient’s follow-up has completed without recurrent atrial fibrillation.

Marrouche NF et al., JAMA. 2014;311:498-506.
MRI Correlation with Voltage Mapping

LVA : < 0.5 mV in SR

Zghaib T et al., JACC Clin Electrophysiol. 2018;4:59-68.
Tailored Atrial Substrate Modification

LVA : < 0.5 mV in SR

Rolf S et al., Circ Arrhythm Electrophysiol. 2014;7:825-33.
Box Isolation of Fibrotic Areas (BIFA)

LVA : < 0.5 mV in SR

Low Voltage Zone Homeogenization

LVZ: 0.1-0.4 mV in SR
Transition zone: 0.4-1.3 mV

Approaches to Low Voltage Area Ablation

Sim I et al., J Interv Card Electrophysiol. 2019
Factors that can influence bipolar voltage

1. Activation vector
2. Angle of incidence
3. Recording electrode size
4. Interelectrode spacing
5. Tissue contact
6. Filtering
7. Mapping density
8. Mapping resolution
# Non-substrate-based Effects upon Bipolar Voltage

<table>
<thead>
<tr>
<th>Factor</th>
<th>Direction of effect on electrogram amplitude (theoretical/pre-clinical)</th>
<th>Direction of effect (clinical)</th>
<th>Clinical demonstration of effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-parallel activation direction</td>
<td>Decrease</td>
<td>–</td>
<td>No</td>
</tr>
<tr>
<td>Increasing angle of incidence</td>
<td>30° improves lesion diagnosis accuracy</td>
<td>–</td>
<td>No</td>
</tr>
<tr>
<td>Increasing electrode size</td>
<td>Variable dependent on tissue</td>
<td>Variable dependent on tissue</td>
<td>Yes</td>
</tr>
<tr>
<td>Increasing electrode spacing</td>
<td>Increase</td>
<td>Increase</td>
<td>Yes</td>
</tr>
<tr>
<td>Increasing tissue contact force</td>
<td>Increase</td>
<td>Increase at low contact force only</td>
<td>Yes</td>
</tr>
<tr>
<td>Bandpass filtering</td>
<td>Effect is based on which filter is applied</td>
<td>Increasing frequency of high pass reduces amplitude</td>
<td>Yes*</td>
</tr>
</tbody>
</table>

*Yes* indicates clinical demonstration, *No* indicates no clinical demonstration.
Electrode Sizes and Spacing

Table 3  Studies comparing catheters with various electrode sizes and spacing

<table>
<thead>
<tr>
<th>Catheter tested</th>
<th>Electrode size (mm²)</th>
<th>Electrode spacing (mm)</th>
<th>Comparator catheter</th>
<th>Electrode size (mm²)</th>
<th>Electrode spacing (mm)</th>
<th>Effect on overall voltage</th>
<th>Effect on LVA size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pentaray</td>
<td>1</td>
<td>2–6</td>
<td>Thermocool</td>
<td>3.5</td>
<td>1–6–2</td>
<td>Increase in scar only</td>
<td>Decrease</td>
</tr>
<tr>
<td>Lasso</td>
<td>1</td>
<td>8</td>
<td>Thermocool</td>
<td>3.5</td>
<td>1–6–2</td>
<td>Increase</td>
<td>Decrease</td>
</tr>
<tr>
<td>Orion Basket</td>
<td>0.4</td>
<td>2.5</td>
<td>Pentaray</td>
<td>1</td>
<td>2–6</td>
<td>–</td>
<td>Unchanged</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lasso</td>
<td>1</td>
<td>1–2</td>
<td>–</td>
<td>Unchanged</td>
</tr>
<tr>
<td>Intella Tip</td>
<td>0.8 (within 4.5 mm tip)</td>
<td>1.2</td>
<td>TactiCath</td>
<td>3.5</td>
<td>2–5–2</td>
<td>–</td>
<td>Increased</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Circular mapping catheter</td>
<td>1</td>
<td>5</td>
<td>–</td>
<td>Unchanged</td>
</tr>
<tr>
<td>Inquiry Optima</td>
<td>1</td>
<td>7</td>
<td>Cool Flex</td>
<td>4</td>
<td>0.5–5–2</td>
<td>–</td>
<td>Decrease</td>
</tr>
</tbody>
</table>
Voltage during AF is Superior to Sinus Rhythm
Directional Sensitivity of Bipolar Recordings

ACTIVATION WAVEFRONT PARALLEL TO THE ELECTRODE PAIR

ACTIVATION WAVEFRONT PERPENDICULAR TO THE ELECTRODE PAIR

Maximum amplitude recorded on bipolar pair

Both electrodes record the same waveform at the same time
→ No difference in unipoles
→ No spike recorded on bipole
Advisor™ HD Grid Mapping Catheter, Sensor Enabled™

16 ELECTRODES ON GRID
- 4 x 4 GRID
- 1 MM ELECTRODE LENGTH

GRID DESIGN COMPOSED OF 4 SPLINES (2.5F)

3-3-3 RING SPACING

COUPLER JOINING FRAMES (NOT AN ELECTRODE)

IRRIGATION PORTS

FLEXABILITY™ CATHETER PLATFORM SHAFT AND HANDLE (8F)
*Minimum 8.5 F introducer

2 ELECTRODES ON DISTAL SHAFT

MAGNETIC SENSORS LOCATED BETWEEN SHAFT ELECTRODES 17 AND 18
The HD Wave Solution

- Unique electrode pattern enables simultaneous measurement of voltage in two directions

- EnSite Precision™ Cardiac Mapping System best duplicate feature uses the highest amplitude EGM for each set of orthogonal bipoles

- In the example to the right, the best duplicate of A1-A2 and A1-B1 will be placed at electrode A1
The HD Wave Solution

HD Wave selects the highest amplitude electrogram from two orthogonal bipoles, reducing directional sensitivity.
Comparison of High-density Voltage Map

CMC, AF
Mean voltage = 0.33 mV
7,842 points

< 0.5mV

< 1.0mV

HD Grid, AF
Mean voltage = 0.41 mV
30,604 points

CMC, HRA pacing
Mean voltage = 1.21 mV
4,039 points

HD Grid, HRA pacing
Mean voltage = 1.55 mV
19,064 points

Yamaguchi T et al., J Atr Fibrillation. 2019;11:2116.
Ablation of Persistent Atrial Fibrillation Targeting Low-Voltage Areas With Selective Activation Characteristics

Amir S. Jadidi, MD; Heiko Lehrmann, MD; Cornelius Keyl, MD; Jérémie Sorrel, MD; Viktor Marksteiner, BSc; Jan Minners, MD; Chan-II Park, MD; Arnaud Denis, MD; Pierre Jais, MD; Mélèze Hocini, MD; Clemens Potocnik, MD; Juergen Allgeier, MD; Willibald Hochholzer, MD; Claudia Herrera-Siklody, MD; Steve Kim, MSEE; Youssef El Omri, MD; Franz-Josef Neumann, MD; Reinhold Weber, MD; Michel Haïssaguerre, MD; Thomas Arentz, MD

Background—Complex-fractionated atrial electrograms and atrial fibrosis are associated with maintenance of persistent atrial fibrillation (AF). We hypothesized that pulmonary vein isolation (PVI) plus ablation of selective atrial low-voltage sites may be more successful than PVI only.

Methods and Results—A total of 85 consecutive patients with persistent AF underwent high-density atrial voltage mapping, PVI, and ablation at low-voltage areas (LVA<0.5 mV in AF) associated with electric activity lasting >70% of AF cycle length on a single electrode (fractionated activity) or multiple electrodes around the circumferential mapping catheter (rotational activity) or discrete rapid local activity (group I). The procedural end point was AF termination. Arrhythmia freedom was compared with a control group (66 patients) undergoing PVI only (group II). PVI alone was performed in 23 of 85 (27%) patients of group I with low amount (<10% of left atrial surface area) of atrial low voltage. Selective atrial ablation in addition to PVI was performed in 62 patients with termination of AF in 45 (73%) after 11±9 minutes radiofrequency delivery. AF-termination sites colocalized within LVA in 80% and at border zones in 20%. Single-procedural arrhythmia freedom at 13 months median follow-up was achieved in 59 of 85 (69%) patients in group I, which was significantly higher than the matched control group (31/66 [47%), \( P<0.001 \)). There was no significant difference in the success rate of patients in group I with a low amount of low voltage undergoing PVI only and patients requiring PVI + selective low-voltage ablation \( (P=0.42) \).

Conclusions—Ablation of sites with distinct activation characteristics within/at borderzones of LVA in addition to PVI is more effective than conventional PVI-only strategy for persistent AF. PVI only seems to be sufficient to treat patients with left atrial low voltage <10%. (Circ Arrhythm Electrophysiol. 2016;9:e002962. DOI: 10.1161/CIRCEP.115.002962.)

Key Words: AF sources • atrial fibrillation • catheter ablation • fibrosis • low voltage • rotational activity
Substrate+EGM guided AF Ablation

Figure 1. A–D, Voltage and regional activation sequence of electrograms on the multielectrode catheter positioned to the anteroseptum of left atrium (LA), where atrial fibrillation (AF) was terminated during later ablation. A, Termination of AF within low voltage (<0.5 mV). Voltage mapping during ongoing AF reveals regions of low voltage (<0.5 mV) at LA anteroseptum. Dark marker between electrode 13 and 15 annotates the site of AF termination by radiofrequency (RF) delivery. B, Orientation of the circumferential mapping catheter at anteroseptal LA. C, Repetitive rotational activity in AF. The regional activation map illustrates the depicted AF beat of D displaying a repetitive sequence of rotational activity on the circumferential mapping catheter at LA anteroseptum (Movie I in the Data Supplement). D, Ablation of electrical activity >70% of AF cycle length terminates AF. Ablation at site of repetitive rotational activity targeting electrodes 13 to 16 with local activation gradient in unipolar recordings (coverage of >70% of AF cycle length on electrodes 7–17) terminates AF to sinus rhythm after 35 s of RF delivery. LAA indicates left atrial appendage; LSPV, left superior pulmonary vein; and RSPV, right superior pulmonary vein. (See also Figures I and II in Data Supplement for identification of rotational activity during ongoing AF.)
Selective Voltage-Guided AF Ablation

Figure 2. Low voltage-guided ablation strategy. Left atrial (LA) low-voltage pattern in patients with persistent atrial fibrillation (AF), assessed by high-density (>800 mapped sites per atrium) multielectrode mapping during ongoing AF. Low-voltage sites were defined as <0.5 mV maximum bipolar voltage. The relative extent of LA low-voltage areas was in A: 3%, B: 24%, C: 46%, and D: 76% of the total LA surface area (with exclusion of the PVs). Radiofrequency energy was applied selectively to low-voltage sites displaying electric activity >70% AF cycle length. CS indicates coronary sinus.
Selective Voltage-Guided AF Ablation

Total persistent AF patients: 85
AA-Drug therapy and electrical CV 10 weeks prior to AF Ablation to induce reverse electrical remodelling

18 pts (22%) in Sinus rhythm
Voltage Mapping in SR / CS-pacing
“PVI-only” as ablation strategy

67/85 pts (79%) in atrial fibrillation
PVI is followed by Ablation of Arrhythmogenic Atrial Fibrosis Sites:
62/85 pts (73%)
AF terminates during PVI:
5/85 pts (7%)

AF terminates during ablation at low voltage sites: 45/62 (73%)
AF terminates to sinus rhythm by PVI + ablation at low voltage sites: 14/45 (31%)
AF terminates to Atrial tachycardia / flutter by PVI + ablation at low voltage sites: 31/45 (69%)

AT-mechanism:
Localized reentry / focal AT: 24/31 (77%)
AT-mechanism:
Macro-reentrant: 7/31 (23%)
Clinical Outcome

Figure 5. Kaplan–Meier curves illustrating freedom from any atrial arrhythmia (A) and freedom from atrial fibrillation (AF; B) at median follow-up (FU) of 13 months (Q1–Q3: 11–15) in patients undergoing PVI+Selective substrate–based ablation vs conventional pulmonary vein isolation (PVI)-only approach. A, Arrhythmia free survival selective voltage-guided ablation vs PVI. B, AF free survival selective voltage-guided ablation vs PVI.
# Trial Outcomes of Substrate-based Ablation

<table>
<thead>
<tr>
<th></th>
<th>Rhythm during mapping</th>
<th>Mapping catheter (electrode size)</th>
<th>Mapping density (mean ± SD points per map)</th>
<th>Control group N (PAF, PsAF)</th>
<th>Study group N (PAF, PsAF)</th>
<th>Control intervention</th>
<th>LVA intervention</th>
<th>F/U (months)</th>
<th>Arrhythmia-free survival (control vs. study)</th>
<th>Additional electrogam features?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schreiber 2017 [5]</td>
<td>Sinus rhythm</td>
<td>Ablation (3.5 mm)</td>
<td>&gt;100</td>
<td>No LVA n=49 (39, 10)</td>
<td>&lt;0.5 mV</td>
<td>PVI alone</td>
<td>PVI + BIFA + L</td>
<td>12</td>
<td>84% vs. 69% P=0.16</td>
<td>None</td>
</tr>
<tr>
<td>Yagishita 2017 [9]</td>
<td>AF</td>
<td>Ablation (3.5 mm)</td>
<td>166±62</td>
<td>No LVA n=42 (15, 27)</td>
<td>&lt;0.5 mV</td>
<td>PVI alone</td>
<td>PVI + HI</td>
<td>12</td>
<td>71% vs. 72% P=0.746</td>
<td>None</td>
</tr>
<tr>
<td>Yamaguchi 2016 [6]</td>
<td>Sinus rhythm</td>
<td>Ablation and mapping (4 mm and 1 mm)</td>
<td>576±150</td>
<td>No LVA n=62 (15, 47)</td>
<td>&lt;0.5 mV &lt;0.5 mV</td>
<td>PVI alone</td>
<td>PVI + HI</td>
<td>32</td>
<td>79% vs. 72% P=0.400</td>
<td>None</td>
</tr>
<tr>
<td>Jadidi 2016 [3]</td>
<td>AF</td>
<td>Mapping (1 mm)</td>
<td>1024±124</td>
<td>Unselected n=66 (0, 66)</td>
<td>PVI alone</td>
<td>PVI + H + RA</td>
<td>PVI + H + RA (further ablation only to terminate AF)</td>
<td>13</td>
<td>47% vs. 69% P&lt;0.001</td>
<td>&lt;0.5 mV, fractionation, rotational activity, rapid local activation</td>
</tr>
<tr>
<td>Yang 2016 [7]</td>
<td>Sinus rhythm</td>
<td>Mapping (1 mm)</td>
<td>628±212</td>
<td>Unselected n=78 (0, 78)</td>
<td>Unselected n=86 (0, 86)</td>
<td>Stepwise</td>
<td>PVI + HI</td>
<td>30</td>
<td>51% vs. 70% P=0.011</td>
<td>&lt;1.3 mV, &gt;50 ms, ≥3 deflections</td>
</tr>
<tr>
<td>Cutler 2016† [4]</td>
<td>Sinus rhythm</td>
<td>Ablation (not stated)</td>
<td>Not stated</td>
<td>Unselected n=76 (0, 76)</td>
<td>Unselected n=65 (0, 65)</td>
<td>PVI + PWI (discretionary)</td>
<td>PVI + PWI</td>
<td>12</td>
<td>57% vs. 80% P=0.005</td>
<td>None</td>
</tr>
<tr>
<td>Kottkamp 2016 [2]</td>
<td>Sinus rhythm</td>
<td>Ablation (4 mm)</td>
<td>100–120</td>
<td>No LVA n=13 (0, 13)</td>
<td>&lt;0.5 mV</td>
<td>PVI alone</td>
<td>PVI + BIFA</td>
<td>12</td>
<td>69% vs. 72% P=0.742</td>
<td>None</td>
</tr>
<tr>
<td>Rolf 2014 [1]</td>
<td>Sinus rhythm</td>
<td>Mapping and ablation (2.1 and 4 mm)</td>
<td>115±35</td>
<td>No LVA n=131 (56, 75) With LVA n=26 (9, 17)</td>
<td>&lt;0.5 mV &lt;0.5 mV</td>
<td>PVI alone</td>
<td>PVI + H + L</td>
<td>12</td>
<td>62% vs. 27% vs. 70%</td>
<td>None</td>
</tr>
</tbody>
</table>

References are highlighted within the table

PVI, pulmonary vein isolation; H, homogenisation; I, isthmus; L, linear; T, transition zone; LVA, low voltage areas; PWI, posterior wall isolation; BIFA, box isolation of fibrotic area; RA, right atrium

Sim I et al., J Interv Card Electrophysiol. 2019
Voltage and Fractionation Map Guided AF Ablation

ClinicalTrials.gov Identifier: NCT03989726

Efficacy of High Density Voltage and Fractionation Map Guided Ablation in Patients With Atrial Fibrillation (INVENTION)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

Sponsor:
Keimyung University Dongsan Medical Center

Collaborator:
Abbott

Information provided by (Responsible Party):
Keimyung University Dongsan Medical Center

Recruitment Status: Not yet recruiting
First Posted: June 18, 2019
Last Update Posted: June 18, 2019

See Contacts and Locations
CFAE and Fractionation Map with HD Grid
LA Voltage Map by Turbomap
LA Voltage Mapping with HD Grid Catheter
Low Voltage and Fractionation Guided Ablation
Case 1

- 58-year-old man
- Longstanding persistent AF (1.5 years)
- AF refractory to amiodarone
- Echo: EF 52%, LAD 4.9 cm, LA volume 130.1 ml
Baseline : AF
LA Voltage and CFAE Mapping
After PV isolation
After LA ablation
Ablation Sites: LA
RA Voltage and CFAE Mapping
AF -> AFL
Ablation Sites
AFL : TCL 250msec
Termination during CTI ablation
Case 2

- 57-year-old woman
- Longstanding persistent AF (1.5 years)
- AF refractory to amiodarone
- Echo: EF 64%, LAD 4.23 cm, LA volume 107.85 ml
LA voltage and fractionation map
Baseline
EGM guided ablation after PVI
AF -> Atypical AFL
Atypical flutter
LA activation map
LA upper ant. wall
CL prolongation during ablation
Tachycardia termination
Ablation sites
Summary

• Low atrial bipolar voltage amplitude is a surrogate marker for the presence of atrial fibrosis, and that atrial fibrosis plays a key role in maintaining AF.

• Patient-specific ablation targeting low voltage area acquired by high-density voltage map could be a promising additional strategy beyond PVI.

• Ablation of sites with distinctive electrogram within low voltage area in addition to PV isolation could be a more effective ablation strategy for persistent AF.
Thanks for your attention !!