New Concept of AF Ablation

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AF ablation, new concept

- New theory
- New clinical trials
- New technique
Challenges in AF Ablation

How to improve success rate
How to improve ablation safety
How to reduce X ray exposure

The Key of AF ablation:
- The correct Ablation Strategy
- Irreversible transmural lesion
AF Mechanism: The key to cure AF

Proper ablation strategy: Base on the mechanism

Reliable ablation: safe, Efficient
AF mechanism and ablation strategy

1914 Garry: “variant circular movement”

1959 Moe: Multiple waves

1985 Alise: experimental study confirmed Moe’s theory

1987 Cox: Cox-Maze Procedure

2001 Jalife: Mother rotor

2005 Yao: single random Reentry: Linear ablation

1997 Jays & Haissagurre: PVI

2000 Pappone: circumferential PVI

2004 Nademanee: CFAEs

2012 Narayan Rotor: Rotor ablation
Evolution of Catheter Ablation Strategies

- **1994**: Focal PV ablation (Haissaguerre, JCE)
- **1996**: Circ. PVI (Pappone, Circulation)
- **2000**: Seg. PVI (Haissaguerre, JCE)
- **2004**: Linear Ablation (Yao, Heart Rhythm)
- **2007**: CFEA (Nademanee, JACC)
- **2012**: Rotor Ablation (Narayan, JACC)
Subset of patients with higher prevalence of non-pulmonary vein triggers

<table>
<thead>
<tr>
<th>Non-paroxysmal AF</th>
<th>Low LVEF</th>
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<tbody>
<tr>
<td>Female gender</td>
<td>Severe LA scarring</td>
</tr>
<tr>
<td>Older age</td>
<td>Hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td>Obesity</td>
<td>Mechanical mitral valve</td>
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<tr>
<td>Sleep apnoea</td>
<td>Late recurrence post-PVAI</td>
</tr>
</tbody>
</table>
Specific regions of non-pulmonary vein triggers

- left atrial posterior wall (PW)
- Other thoracic veins
  - superior vena cava (SVC)
  - Coronary sinus (CS)
  - Vein of Marshall
- Crista terminalis (CR)
- Interatrial septum (IAS)
- Left atrial appendage (LAA)
### Selected studies on catheter ablation of non-PV

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</thead>
<tbody>
<tr>
<td>Lumia et al.</td>
<td>2018</td>
<td>407</td>
<td>PAF: 51% PrAF: 10% Permanent AF: 39%</td>
<td>PAF: 100%</td>
<td>PAF: 100%</td>
<td>PAF: 33% PrAF: 67%</td>
<td>NA</td>
<td>LSPAF: 100%</td>
<td>103</td>
</tr>
<tr>
<td>Kukiyama et al.</td>
<td>2017</td>
<td>320</td>
<td>PAF: 46% PrAF: 23% Permanent AF: 31%</td>
<td>PAF: 100%</td>
<td>PAF: 100%</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Tamborero et al.</td>
<td>2016</td>
<td>68</td>
<td>PAF: 100%</td>
<td>Focal ablation (32 patients) and segmental isolation (36 patients)</td>
<td>Prospective cohort (SVIA + SVC isolation ± CTI line, other non-PV triggers)</td>
<td>Prospective cohort (SVIA + as-needed SVC isolation ± CTI line, other non-PV triggers vs. SVIA + empirical SVC isolation ± CTI line, other non-PV triggers)</td>
<td></td>
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<tr>
<td>Lim et al.</td>
<td>2015</td>
<td>186</td>
<td>PAF: 100%</td>
<td></td>
<td>Prospective cohort (SVIA + CS isolation ± roof MI line, LA CFAE ablation)</td>
<td></td>
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</tr>
<tr>
<td>Kim et al.</td>
<td>2014</td>
<td>45</td>
<td>PAF: 33% PrAF: 67%</td>
<td></td>
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</table>

**Notes:**
- RCT (PVI + SVC isolation—empirical in 217 patients)
- Segmental isolation 450 days 84%
- Segmental isolation 12 months 74% vs. 81% (NS)
- Focal ablation (32 patients) and segmental isolation (36 patients) 65%
- Prospective cohort (SVIA + SVC isolation ± CTI line, other non-PV triggers) 56% vs. 77%
- Prospective cohort (SVIA + as-needed SVC isolation ± CTI line, other non-PV triggers vs. SVIA + empirical SVC isolation ± CTI line, other non-PV triggers) 51% vs. 74%
- Isolation 78%
- Isolation 51% vs. 74%
- Prospective cohort (AF ablation + focal CS ablation vs. AF ablation + CS isolation) 56% vs. 76%
The role of non-pulmonary vein triggers in AF ablation

- Ablation of non-PV triggers is an important step to improve outcomes in AF ablation
- Non-pulmonary vein triggers typically originates from predictable sites (such as the left atrial PW, SVC, CS, IAS, CR)
- These areas can be ablated either empirically or after observing significant ectopy (with or without drug challenge)
Rotor mapping and ablation

Treatment of Atrial Fibrillation by the Ablation of Localized Sources

CONFIRM (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation) Trial

Sanjiv M. Narayan, MD, PhD, David E. Krummen, MD, Kalyanam Shivkumar, MD, Paul Clopton, MS, Wouter-Jan Rappel, PhD, John M. Miller, MD

San Diego and Los Angeles, California; and Indianapolis, Indiana

Figure 4 Cumulative Freedom From Primary Endpoint
Acute and early outcomes of focal impulse and rotor modulation (FIRM)-guided rotors-only ablation in patients with nonparoxysmal atrial fibrillation

Carola Gianni, MD,† Sanghamitra Mohanty, MD, MS, FHRS,*, Luigi Di Biase, MD, PhD, FHRS,†‡ Tamara Metz, RN, BSN, Chintan Trivedi, MD, Yalçın Gökoğlan, MD,‡ Mahmut F. Güneş, MD,‡ Rong Bái, MD, FHZ, Amin Al-Ahmad, MD, CCDS, FHZ,‡ J. David Burkhardt, MD, FHZ, G. Joseph Galligouline, MD, FHZ,‡ Rodney P. Horton, MD, FHZ,§ Patrick M. Hranitzky, MD, FHZ, Gayle E. Sanchez, MD,§ Philipp Halbbaß, MD,§ Patrick Müller, MD,§ Anja Schade, MD,§ Thomas Denoeke, MD, PhD, FHZ,§**, Gery F. Tomassoni, MD, FHZ,§ Andrea Natale, MD, FHZ†‡§

From the †Texas Cardiac Arrhythmia Institute, St. David's Medical Center, Austin, Texas, ‡Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy, §Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York, §Department of Biomedical Engineering, University of Texas, Austin, Texas, †Department of Clinical and Experimental Medicine, University of Foggia, Foggia, Italy, ‡Department of Cardiology, Gülhane Military Academy of Medicine, Ankara, Turkey, §Clinic for Interventional Electrophysiology, Heart Center Bad Neustadt, Bad Neustadt, Germany, ††University Hospital Bergmannsheil, Ruhr University Bochum, Bochum, Germany, ††Baptist Health Lexington, Lexington, Kentucky, ‡‡Division of Cardiovascular Diseases, Scripps Clinic, La Jolla, California, ††MetroHealth Medical Center, Case Western Reserve University School of Medicine, Cleveland, Ohio, ‡Clinical Electrophysiology and Arrhythmia Services, California Pacific Medical Center, San Francisco, California, and ‡‡Dell Medical School, University of Texas, Austin, Texas.

BACKGROUND: Focal impulse and rotor modulation (FIRM)-guided ablation targets sites that are thought to sustain atrial fibrillation (AF).

OBJECTIVE: The purpose of this study was to evaluate the acute and mid-term outcomes of FIRM-guided only ablation in patients with nonparoxysmal AF.

METHODS: We prospectively enrolled patients with persistent and long-standing persistent (LSP) AF at three centers to undergo FIRM-guided only ablation. We evaluated acute procedural success (defined as AF termination, organization, or ≥10% slowing), safety (incidence of periprocedural complications), and long-term success (single-procedure freedom from atrial tachycardia [AT]/AF off antiarrhythmic drugs [AAD] after a 2-month blanking period).

RESULTS: Twenty-six patients were included (mean age 70±12 years; 58% male; 77% paroxysmal and 23% persistent). Of those, 24 patients were enrolled and randomized in this study. The acute clinical success rate was 100% with 100% freedom from AF at the 2-month follow-up. The procedural success rate was 92%.

CONCLUSION: In nonparoxysmal AF patients, targeted ablation of FIRM-identified rotors is effective in obtaining AF termination, organization, or slowing during the procedure. After mid-term follow-up, the strategy of ablation FIRM-identified rotors alone did not prevent recurrence from AT/AF.

KEYWORDS: Atrial fibrillation; Catheter ablation; Rotor; FIRM mapping;
Real-time dominant frequency analysis in patients with PeAF
Dominant frequency analysis in patients with PeAF

- Method: Matlab;
- Activation of virtual unipolar activation in every point was analyzed, the frequency was calculated by the negative peak; The ventricular activation and potential electromagnetic interference was excluded.

(A) Spectrum distribution in an individual LA from Antero-superior, right and left lateral views.
Atrial fibrillation ablation using very short duration 50 W ablations and contact force sensing catheters

Roger A. Winkle1,2, Ryan Moskovitz3, R. Hardwin Mead1, Gregory Engel1, Melissa H. Kong1, William Fleming1, Jonathan Salcedo1, Rob A. Patrawala1, John H. Tranter3, Isaac Shal1

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Abstract

Purpose The optimal radiofrequency (RF) power and lesion duration using contact force (CF) sensing catheters for atrial fibrillation (AF) ablation are unknown. We evaluate 50 W RF power for very short durations using CF sensing catheters during AF ablation.

Methods We evaluated 51 patients with paroxysmal (n = 20) or persistent (n = 31) AF undergoing initial RF ablation.

Results A total of 3961 50 W RF lesions were given (average 77.6 ± 19.1/patient) for an average duration of only 11.2 ± 3.7 s. As CF increased from < 10 to > 40 g, the RF application duration decreased from 13.7 ± 4.4 to 8.6 ± 2.5 s (p < 0.0005). Impedance drops occurred in all ablations, and for patients in sinus rhythm, there was loss of pacing capture during RF delivery suggesting lesion creation. Only 3% of the ablation lesions were at 5 g and 1% at > 40 g of force. As CF increased, the force time integral (FTI) increased from 47 ± 24 to 376 ± 102 gs (p < 0.0005) and the lesion index (LSI) increased from 4.10 ± 0.51 to 7.63 ± 0.50 (p < 0.0005). Both procedure time (101 ± 19.7 min) and total RF energy time (895 ± 258 s) were very short. For paroxysmal AF, the single procedure freedom from AF was 86% at 1 and 2 years. For persistent AF, it was 83% at 1 year and 72% at 2 years. There were no complications.

Conclusions Short duration 50 W ablations using CF sensing catheters are safe and result in excellent long-term freedom from AF for both paroxysmal and persistent AF with short procedure times and small amounts of total RF energy delivery.

Keywords Atrial fibrillation - AF ablation - Contact force catheters

Fig. 6 Kaplan-Meier curves showing the single procedure freedom from AF by AF type (red = paroxysmal AF and green = persistent AF)
50W, “Omega” line + anterior wall line converts persistent AF to SR
low voltage zone outside PV ostium predict high recurrence of PVI

Qiao Y, Yao Y et al. JAHA. 2015.
Individualized Ablation Strategy

- **Paroxysmal AF**
  - PV Isolation
  - Voltage mapping guided modification

- **Persistent AF**
  - PV Isolation
  - Linear ablation
Clinical Trial

Purpose of CABANA

Compare Ablation to state-of-the-art drug therapy for patients with new onset / undertreated AF

Primary Endpoint

- All-cause mortality, disabling stroke, serious bleeding, or cardiac arrest

Major Secondary Endpoints

- All-cause mortality
- Death (all-cause) or cardiovascular hospitalization
Patient Randomization

Subjects 2204

Ablation Therapy 1108

- Ablated 1006 (90.8%)
  - Repeat ablation 215 (19.4%)
- Not ablated 102 (9.2%)

Completed FU 1002 (90.4%) 48.9 mo

Drug Therapy 1096

- Drug Treated 1092 (99.6%)
  - Rhythm control 953 (87.2%)
  - Rate control only 126 (11.5%)
- Cross Over Ablated 301 (27.5%)
- Completed FU 966 (88%) 48.2 mo
Estimates of All-Cause Mortality Risk (ITT)

Ablation vs. Drug
Hazard ratio: 0.85 (95% CI, 0.60–1.21)
P=0.377
All-Cause Mortality or Cardiovascular Hospitalization (ITT)

Ablation vs. Drug
Hazard ratio: 0.83 (95% CI, 0.74–0.93)
P=0.002

Number at risk
Drug
Ablation
1096
1108
778
807
643
708
563
643
474
558
387
450
302
372
244
261
197
165
112

Months since randomization
Event rate (%)
First Recurrence AF – Post Blanking* (ITT)

Ablation vs. Drug
Hazard ratio: 0.53 (95% CI, 0.46–0.61)
P<0.0001
Conclusion of CABANA

- Ablation did not produce a significant reduction in the primary endpoint and all-cause mortality
- The results were affected by cross-overs in both directions and lower than expected event rates
- Ablation significantly reduced mortality or CV hospitalization by 17% compared to drug therapy
- There also was a significant 47% reduction in recurrent AF with ablation compared to drug therapy
- A 33% reduction in the primary endpoint and 40% mortality risk reduction was present when patients actually underwent ablation (treatment received)
Effect of Catheter Ablation vs Medical Therapy on Quality of Life Among Patients With AF--CABANA

Figure 2. Atrial Fibrillation Effect on Quality of Life (AFEQT) Summary Scores

A Mean AFEQT summary score

B Between-group AFEQT summary score difference

<table>
<thead>
<tr>
<th>Interval, mo</th>
<th>No. of Patients Ablation (n=1108)</th>
<th>No. of Patients Drug Rx (n=1096)</th>
<th>Adjusted Mean Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>1084</td>
<td>1078</td>
<td>-0.2 (-1.9 to 1.5)</td>
</tr>
<tr>
<td>3</td>
<td>971</td>
<td>983</td>
<td>3.0 (1.3 to 4.7)</td>
</tr>
<tr>
<td>12</td>
<td>915</td>
<td>903</td>
<td>5.3 (3.7 to 6.9)</td>
</tr>
<tr>
<td>24</td>
<td>856</td>
<td>798</td>
<td>4.3 (2.7 to 6.0)</td>
</tr>
<tr>
<td>36</td>
<td>645</td>
<td>605</td>
<td>2.5 (0.8 to 4.1)</td>
</tr>
<tr>
<td>48</td>
<td>476</td>
<td>473</td>
<td>3.0 (1.1 to 4.9)</td>
</tr>
<tr>
<td>60</td>
<td>329</td>
<td>320</td>
<td>2.6 (0.3 to 4.8)</td>
</tr>
<tr>
<td>All</td>
<td>4192</td>
<td>4082</td>
<td>3.4 (2.1 to 4.8)</td>
</tr>
</tbody>
</table>

JAMA. 2019 Mar 15. doi: 10.1001
Effect of Catheter Ablation vs Medical Therapy on Quality of Life Among Patients With AF—CABANA

Figure 3. Mayo Atrial Fibrillation-Specific Symptom Inventory (MAFSI) Frequency Scores

A Mean MAFSI frequency score

B Between-group MAFSI frequency score difference

<table>
<thead>
<tr>
<th>Interval, mo</th>
<th>No. of Patients Ablation (n=1108)</th>
<th>No. of Patients Drug Rx (n=1096)</th>
<th>Adjusted Mean Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>1069</td>
<td>1061</td>
<td>-0.2 (-0.7 to 0.4)</td>
</tr>
<tr>
<td>3</td>
<td>897</td>
<td>894</td>
<td>-1.6 (-2.2 to -1.0)</td>
</tr>
<tr>
<td>12</td>
<td>828</td>
<td>831</td>
<td>-1.7 (-2.3 to -1.2)</td>
</tr>
<tr>
<td>24</td>
<td>759</td>
<td>724</td>
<td>-1.7 (-2.3 to -1.1)</td>
</tr>
<tr>
<td>36</td>
<td>571</td>
<td>559</td>
<td>-1.2 (-1.9 to -0.6)</td>
</tr>
<tr>
<td>48</td>
<td>424</td>
<td>419</td>
<td>-0.8 (-1.6 to -0.1)</td>
</tr>
<tr>
<td>60</td>
<td>279</td>
<td>295</td>
<td>-1.3 (-2.1 to -0.5)</td>
</tr>
<tr>
<td>All</td>
<td>3758</td>
<td>3722</td>
<td>-1.4 (-1.9 to -0.9)</td>
</tr>
</tbody>
</table>

Favors Drug Therapy: --

Favors Catheter Ablation: --

Adjusted Mean Difference (95% CI)

JAMA. 2019 Mar 15. doi: 10.1001
Catheter Ablation for Atrial Fibrillation with Heart Failure

Nassir F. Marrouche, M.D., Johannes Brachmann, M.D., Dietrich Andresen, M.D., Jürgen Siebels, M.D., Lucas Boersma, M.D., Luc Jordaens, M.D., Béla Merkely, M.D., Evgeny Pokushalov, M.D., Prashanthan Sanders, M.D., Jochen Proff, B.S., Heribert Schunkert, M.D., Hildegard Christ, M.D., Jürgen Vogt, M.D., and Dietmar Bänsch, M.D., for the CASTLE-AF Investigators*
Catheter Ablation Was Associated With A Significantly Lower Rate Of A Composite End Point Of Death From Any Cause Or Hospitalization For Worsening Heart Failure Than Was Medical Therapy

A
B
C

Death or Hospitalization for Worsening

No. at Risk
Ablation Medical therapy
179 184
141 145

Hospitalization for Worsening Heart Failure

No. at Risk
Ablation Medical therapy
179 184
141 145

Hazard ratio, 0.62 (95% CI, 0.43–0.88) P = 0.007 by Cox regression

Hazard ratio, 0.56 (95% CI, 0.37–0.83) P = 0.004 by Cox regression

P = 0.006 by log-rank test

P = 0.004 by log-rank test
Endo-/Epicardial Catheter Ablation Of AF

Feasibility, Outcome, And Insights Into Arrhythmia Mechanisms

59 patients with AF / AT despite durable PV isolation

14% purely epicardial low voltage
19% further epicardial conduction abnormalities
80% epicardial ablation for transmurality
73% freedom from recurrences over 23 ± 10 months of continuous follow-up

biatrial endo- and epicardial SR voltage map and targeted ablation
Epi-Edo low voltage substrates
Epicardial conduction abnormalities in (SR)—associated to the epicardial fiber network
Epicardial connection between RA and LA through BB
Epicarial Role In AF Ablation

- Enabled detection of exclusive epicardial low voltage substrates
- Improved transmurality of linear ablation lesions
- Revealed conduction abnormalities located in the epicardial fiber network and their role in the development of atrial fibrillation reentry mechanisms
Should we Routinely map Edo/Epi of Atrium

- Time consuming:
  - Procedure duration measured 174±55 minutes
  - Fluoroscopy time was 36±12 minutes.

- Complications:
  - No complication was associated with the epicardial access route
  - Failed AF ablation patients
New technique

**Pulsed Field Ablation for Pulmonary Vein Isolation in Atrial Fibrillation**

![Diagram showing pulmonary vein isolation](image)

<table>
<thead>
<tr>
<th>First-in-Human IMPULSE &amp; PEFCAT Trials</th>
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<tbody>
<tr>
<td><strong>Trials enrolled 81 Paroxysmal AF patients:</strong></td>
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<tr>
<td>- Successful PV isolation with PFA in 100%</td>
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<td>- Total procedure time = 92.2 ± 27.4 min</td>
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<td>- PFA catheter dwell time = 33.7 ± 16.6 min</td>
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<tr>
<td><strong>Invasive Remapping at ~ 3 months:</strong></td>
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<td>- Biphasic-3 Waveform: 18 pts remapped</td>
</tr>
<tr>
<td>- 100% of PVs durably isolated</td>
</tr>
<tr>
<td><strong>Favorable Safety Profile:</strong></td>
</tr>
<tr>
<td>- No esophageal damage</td>
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<tr>
<td>- No pulmonary vein stenosis / narrowing</td>
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<tr>
<td>- No phrenic nerve injury</td>
</tr>
</tbody>
</table>

The 12-month Kaplan-Meier estimate of freedom from arrhythmia was $87.4 \pm 5.6\%$
New technique

Apama RF Balloon Catheter System for the treatment of AF

MRI-guided EP ablation labs
Conclusion

• Ablation of PeAF is still a challenge due to the uncertain mechanism

• Ablation of non-PV triggers is an important step to improve outcomes in AF ablation

• Catheter-based endo-/epicardial mapping and ablation of AF was feasible and safe indicating potential further development of current AF treatment.

• Pulsed field ablation is a novel ablation modality that demonstrates preferential myocardial ablation without damage to adjacent structures, exhibits durable PV isolation when using an optimized biphasic waveform.
Thank you for your attention
**Supplemental Table S3: Details of the Various Waveform Cohorts**

<table>
<thead>
<tr>
<th></th>
<th>Monophasic</th>
<th>Biphasic-1</th>
<th>Biphasic-2</th>
<th>Biphasic-3</th>
<th>Biphasic-3x</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Waveform polarity</strong></td>
<td>Monophasic</td>
<td>Biphasic</td>
<td>Biphasic</td>
<td>Biphasic</td>
<td>Biphasic</td>
</tr>
<tr>
<td><strong>No. of heartbeats over which pulses are delivered</strong></td>
<td>4</td>
<td>10</td>
<td>8</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td><strong>Catheter pose</strong></td>
<td>Flower</td>
<td>Flower</td>
<td>Flower and Basket</td>
<td>Flower and Basket</td>
<td>Flower and/or Basket</td>
</tr>
</tbody>
</table>

* Waveform composition refers to the proprietary details of the actual pulse sequence.