New Technologies for Catheter Ablation of Atrial Fibrillation

Karl H Kuck
Aklepios Klinik St. Georg
Hamburg, Germany
<table>
<thead>
<tr>
<th>Disclosure Statement</th>
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<tbody>
<tr>
<td><strong>Research Grants</strong></td>
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<td><strong>Speaker’s Bureau Honoraria</strong></td>
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<td><strong>Fellowship Support</strong></td>
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<tr>
<td><strong>Other</strong></td>
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<td><strong>Off-label drugs/devices</strong></td>
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</tbody>
</table>
Catheter ablation of atrial fibrillation

Agenda

- PV’s – complete isolation: GAPAF Trial
- Durable PVI
  - Contact force
  - Laser
  - Cryo
- Mechanisms in persistent/longstanding persistent AF
  - Rotors
- Role of autonomic nervous system
Catheter ablation of atrial fibrillation

**Agenda**

- PV´s – complete isolation: GAPAF Trial
- Durable PVI
  - Contact force
  - Laser
  - Cryo
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  - Rotors
Catheter ablation of atrial fibrillation

Irrigated tip, max 30 W in posterior wall and roof, max 40 W at other sites

Ouyang et al, Circulation 2004
Atrial Fibrillation - Catheter ablation

The mean follow-up period was 14 months, with a range from 2 to 30 months.

## Major Complications

<table>
<thead>
<tr>
<th>Type of Complication</th>
<th>No of Pts</th>
<th>Rate,%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>25</td>
<td>0.15</td>
</tr>
<tr>
<td>Tamponade</td>
<td>213</td>
<td>1.31</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>15</td>
<td>0.09</td>
</tr>
<tr>
<td>Haemothorax</td>
<td>4</td>
<td>0.02</td>
</tr>
<tr>
<td>Sepsis, abscesses or endocarditis</td>
<td>2</td>
<td>0.01</td>
</tr>
<tr>
<td>Permanent diaphragmatic paralysis</td>
<td>28</td>
<td>0.17</td>
</tr>
<tr>
<td>Total femoral pseudoaneurysm</td>
<td>152</td>
<td>0.93</td>
</tr>
<tr>
<td>Total artero-venous fistulae</td>
<td>88</td>
<td>0.54</td>
</tr>
<tr>
<td>Valve damage/requiring surgery</td>
<td>11/7</td>
<td>0.07</td>
</tr>
<tr>
<td>Atrium-esophageal fistula</td>
<td>3</td>
<td>0.02</td>
</tr>
<tr>
<td>Stroke</td>
<td>37</td>
<td>0.23</td>
</tr>
<tr>
<td>Transient ischaemic attack</td>
<td>115</td>
<td>0.71</td>
</tr>
<tr>
<td>Pulmonary veins stenoses requiring intervention</td>
<td>48</td>
<td>0.29</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>741</strong></td>
<td><strong>4.54</strong></td>
</tr>
</tbody>
</table>

R. Cappato et al, JACC 2009
Catheter ablation of atrial fibrillation

- 95% of pts with AF recurrence after PV isolation have gaps despite previous isolation
- Re-ablation of conducting gaps leads to SR in follow-up

• Complete PVI
## Persistent PVI – Results of Remapping

<table>
<thead>
<tr>
<th>Procedure</th>
<th>PV spike in any PV, n [%]</th>
<th>PV spike in sept. PVs, n [%]</th>
<th>Spike in lat. PVs, n [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>2\textsuperscript{nd} procedure [n=101]</td>
<td>81 [80%]</td>
<td>54 [53%]</td>
<td>65 [64%]</td>
</tr>
<tr>
<td>3\textsuperscript{rd} procedure [n=26]</td>
<td>7 [27%]</td>
<td>5 [19%]</td>
<td>6 [23%]</td>
</tr>
<tr>
<td>4\textsuperscript{th} procedure [n=7]</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5\textsuperscript{th} procedure [n=1]</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Tilz, Ouyang et al. JCE 2010
GAP-AF

Group A: Single Gap
stop ablation immediately after PV-isolation to allow re-conduction

Group B:
complete linear PV-isolation

Follow up using telemetry
Recurrence: symptomatic AFib or asymptomatic AFib defined as 2 consecutive AFib recordings in 3 following days

Invasive re-check after 3 months (or earlier depending on patient’s symptoms)

Kuck KH et al, Circ AE in press
GAP-AF

Invasive re-check after 3 months
(or earlier depending on patient’s symptoms)

No AFib recurrence

PV isolated

Only diagnostic EP study

PV not isolated

AFib recurrence

PV isolated

Add lines/ Focus ablation

PV not isolated

PV re-isolation

Kuck KH et al, Circ AE in press
Gap – AF Primary Endpoint

Kuck KH et al, Circ AE in press
**Gap – AF**: *incomplete group – complete group
FU EP study*

- **Incomplete group**
  - n = 103
  - Pts with gaps
    - n = 92 (89.3%)

- **Complete group**
  - n = 93
  - Pts with gaps
    - n = 65 (69.9%)

*Kuck KH et al, Circ AE in press*
Catheter ablation of atrial fibrillation

**Agenda**

- PV´s – complete isolation: GAPAF Trial
- Durable PVI
  - Contact force
  - Laser
  - Cryo
- Mechanisms in persistent/longstanding persistent AF
  - Rotors
Contact Force Technologies

TactiCath, St Jude Medical

SmartTouch, Biosense Webster
General principle Contact Force sensor

- Deformable body between shaft and tip
- Micro-movements are detected
  - Optical principle
  - Magnetic principle
- Recalculation of tip CF that originates the micro-movements
TactiCath Technology

- Optical module emits light in the fiber optic
- Reflected light depends on tip micro-movements

- No calibration:
- **50Hz sampling rate** to provide real-time highly accurate information on CF
Proof of Concept model 3: closed chest beating heart

Ikeda, Nakagawa, et al., Circ Arrh & EP,
DOI: 10.1161/CIRCEP.113.001094, 7 Nov 2014
TOCCATA
- Feasibility & safety of contact force sensing
- Chronic success related to Contact Force

EFFICAS I
Electrical reconnection correlates with:
- Minimum Contact Force
- Minimum Force Time Integral

EFFICAS II
Contact Force guidelines improve EP outcome

TOCCASTAR IDE Study
Prospective randomized safety & efficacy pivotal trial

Clinical studies

PATH TO CONTACT FORCE RECOMMENDATIONS
Significant Force Variability by Operator

Kuck et al. A novel radiofrequency ablation catheter using contact force sensing: Toccata study.
Heart Rhythm 2012 Jan;9(1):18-23
Contact Force predicts Clinical outcome for AF

Percentage of Non-Successful & Successful Isolation as a function of average Contact Force

- 0 – 10 g (n=5): 100% No success
- 10 – 20 g (n=17): 47% Success, 53% No success
- 20+ g (n=10): 80% Success, 20% No success

Each Lesion: Target Force >20 g Do not ablate <10g

AF patient outcome at 12 months correlates to average CF (p=0.013)

Minimum FTI is a strong determinant for durable lesion formation

Each ablation should be made with FTI > 400 g.s!

Neuzil P, et al. Electrical Reconnection Following PVI is Contingent on Contact Force during Initial Treatment - Results From the EFFICAS I Study. Circ Arrhythm Electrophysiol 2013;6;327-333
EFFICAS II: improved durable PV isolation

Long-term isolation can be achieved in 85% of the veins when ablated following contact force recommendations.

Kautzner J… Kuck KH. Europace (2015) 17, 1229–1235

EFF1 n=26 patients
EFF2 n=24 patients
EFFICAS II: improved durable PV isolation

Long-term isolation can be achieved in 85% of the veins when ablated following contact force recommendations.

Kautzner J... Kuck KH. Europace (2015) 17, 1229–1235

EFF1 n=26 patients
EFF2 n=24 patients
# Trial Design

| Design | Prospective, 1:1 randomized, multicenter non-inferiority study  
|        | Test device (CF) - TactiCath™ Contact Force (CF) sensing RFA catheter (St. Jude Medical)  
|        | Control device (CTL) – Navistar™ Thermocool™ (Biosense Webster)  
|        | Sample Size: 300 randomized PAF subjects treated with PVI (+17 roll in CF group)  
|        | 3 month blanking, 12 month total follow-up  
|        | 17 sites (10 US, 7 EU); 47 operators |

| Analyses | Primary Effectiveness - CF is non-inferior to CTL (off-drug symptomatic recurrence of atrial arrhythmia lasting > 30s)  
|          | Primary Safety - CF is non-inferior to CTL (early onset device related serious adverse events)  
|          | Descriptive endpoints – protocol specified analyses of CF utilization |

| Status | Conducted under Investigational Device Exemption (IDE)  
|        | 12 month follow-up complete June 2013  
|        | Currently under regulatory review |

| Sponsor | St. Jude Medical, St. Paul, MN  
|         | Study initiated under Endosense, Geneva, Switzerland |
## Participating Sites

### United States

<table>
<thead>
<tr>
<th>Institution</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mount Sinai Medical Center</td>
<td>New York, New York</td>
</tr>
<tr>
<td>Mass General Hospital</td>
<td>Boston, Massachusetts</td>
</tr>
<tr>
<td>Texas Cardiac Arrhythmia Research</td>
<td>Austin, Texas</td>
</tr>
<tr>
<td>Brigham &amp; Women’s Hospital</td>
<td>Boston, Massachusetts</td>
</tr>
<tr>
<td>Medical College of South Carolina</td>
<td>Charleston, South Carolina</td>
</tr>
<tr>
<td>Cleveland Clinic</td>
<td>Cleveland, Ohio</td>
</tr>
<tr>
<td>University of Pennsylvania</td>
<td>Philadelphia, Pennsylvania</td>
</tr>
<tr>
<td>University of Virginia</td>
<td>Charlottesville, Virginia</td>
</tr>
<tr>
<td>Ohio State University</td>
<td>Columbus, Ohio</td>
</tr>
<tr>
<td>Mayo Clinic</td>
<td>Rochester, Minnesota</td>
</tr>
</tbody>
</table>

### Europe

<table>
<thead>
<tr>
<th>Institution</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital na Homolce</td>
<td>Prague, Czech Republic</td>
</tr>
<tr>
<td>Clinique Pasteur</td>
<td>Toulouse, France</td>
</tr>
<tr>
<td>Institute for Clinical and Experimental Medicine</td>
<td>Prague, Czech Republic</td>
</tr>
<tr>
<td>Hopital Universitaire de Geneve</td>
<td>Geneva, Switzerland</td>
</tr>
<tr>
<td>Asklepios Klinik St. Georg</td>
<td>Hamburg, Germany</td>
</tr>
<tr>
<td>San Raffaele Hospital</td>
<td>Milan, Italy</td>
</tr>
<tr>
<td>Erasmus Medical Center</td>
<td>Rotterdam, Netherlands</td>
</tr>
</tbody>
</table>

The TactiCath Quartz Set is currently undergoing FDA review for premarket approval.

CAUTION: Investigational device in the United States. Limited by Federal (or U.S.) law to investigational use. Not available for sale in the U.S.
Primary Effectiveness Endpoint Met

- Non-inferiority of TactiCath to CTL was demonstrated if the 95% LCB for the difference in rates (TactiCath minus CTL) was greater than -15%

<table>
<thead>
<tr>
<th></th>
<th>TactiCath (N=146)</th>
<th>Control (N=134)</th>
<th>Difference [95% LCB]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic success</td>
<td>99 (67.8%)</td>
<td>93 (69.4%)</td>
<td>-1.6% [-10.7%]</td>
</tr>
<tr>
<td>(12 month)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Primary effectiveness based on per protocol cohort (280 patients; 93.3% of randomized subjects)

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Per protocol, physicians were not required to target a specific amount of contact force

- Analysis of contact force data showed differences within the TactiCath cohort
  “Optimal CF” cohort: ≥ 90% lesions delivered at ≥10g of contact force


2. Contact force data available unavailable for 1 patient

3. Optimal CF cohort defined as those patients where ≥ 90% lesions ≥10g

4. Non-optimal CF cohort defined as those patients where < 90% lesions ≥10g

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Protocol-Specified Descriptive Endpoint Analysis:
Optimal CF Impact on Success and Repeat Ablations

Optimal CF\textsuperscript{2} vs. Non-optimal CF\textsuperscript{3} Clinically Relevant Success at 12 months

<table>
<thead>
<tr>
<th>Success Rate</th>
<th>Optimal CF</th>
<th>Non-optimal CF</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 months</td>
<td>85.5%</td>
<td>67.7%</td>
</tr>
</tbody>
</table>

\( p = 0.01 \)

Contact Force and Control:
Rate of Repeat Ablation\textsuperscript{1}

- Optimal CF\textsuperscript{2}
  - Rate: 4.8%
  - \( p = 0.04 \)

- Control
  - Rate: 12.7%
  - \( p = 0.02 \)

- Non-optimal CF\textsuperscript{3}
  - Rate: 16.1%

1. Repeat ablation after the protocol defined 3 month blanking period; protocol defined success used for analysis
2. Optimal CF cohort defined as those patients where ≥ 90% lesions ≥10g
3. Non-optimal CF cohort defined as those patients where < 90% lesions ≥10g

The TactiCath Quartz Set is currently undergoing FDA review for premarket approval

CAUTION: Investigational device in the United States. Limited by Federal (or U.S.) law to investigational use. Not available for sale in the U.S.
SMART-AF Trial

Paroxysmal AF Catheter Ablation With a Contact Force Sensing Catheter

Results of the Prospective, Multicenter SMART-AF Trial

Andrea Natale, MD,*†∥∥∥ Vivek Y. Reddy, MD,# George Monir, MD,** David J. Wilber, MD,†† Bruce D. Lindsay, MD,‡‡ H. Thomas McElderry, MD,§§ Charan Kantipudi, MD,¶¶ Moussa C. Mansour, MD,¶¶ Daniel P. Melby, MD,## Douglas L. Packer, MD,** Hiroshi Nakagawa, MD,††† Baohui Zhang, MS, SM,††† Robert B. Stagg, PhD,††† Lee Ming Boo, PharmD,††† Francis E. Marchlinski, MD§§§
SMART-AF Trial

Figure 2: Kaplan-Meier curve of time to first atrial fibrillation/atrial flutter/atrial tachycardia recurrence (effectiveness cohort, n = 122).

A Natale et al, J Am Coll Cardiol 2014;64:647–56
SMART-AF Trial

A Natale et al, J Am Coll Cardiol 2014;64:647–56
SMART-AF Trial

![Bar chart](chart.png)

**FIGURE 4** Distribution of Percentage of Time With CF Within Investigator-Selected Working Range

A Natale et al, J Am Coll Cardiol 2014;64:647–56
SMART-AF Trial

**Figure 5** Kaplan-Meier Curve of Time to First Atrial Fibrillation/Atrial Flutter/Atrial Tachycardia Recurrence Through 12 Months

A Natale et al, J Am Coll Cardiol 2014;64:647–56
## SMART-AF Trial

<table>
<thead>
<tr>
<th>Dataset</th>
<th>No. of Pts</th>
<th>12-Month Success (AF/AT-free)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMART-AF (≥80% time within preselected contact force range)</td>
<td>51</td>
<td>81%</td>
</tr>
<tr>
<td>SMART-AF (&lt;80% time within preselected contact force range)</td>
<td>57</td>
<td>66%</td>
</tr>
<tr>
<td>Non Force-Sensing Open-Irrigated Catheter*</td>
<td>106</td>
<td>66%</td>
</tr>
</tbody>
</table>

**CENTRAL ILLUSTRATION**  
Outcomes Comparison With Various Types and Forces of Ablation Catheters

A Natale et al, J Am Coll Cardiol 2014;64:647–56
Catheter ablation of atrial fibrillation

**Agenda**

- Role of PV´s
- Durable PVI
  - Contact force
  - Laser
  - Cryo
- Mechanisms in persistent/longstanding persistent AF
  - Rotors
- Role of autonomic nervous system
Biophysics of Cryoballoon Ablation

- Extracellular ice formation results in osmotic shifts and cellular dehydration.
- Uniform intracellular ice formation leads to irreversible organelle damage.
- Thawing leads to further damage via acute extracellular hypotonicity (melting ice), hyperemia, and vascular leak.
Principles of Cryoballoon Ablation
Online PV Signal Registration
The First-Generation Cryoballoon

7mm
Procedure Experience Impacts Treatment Success: STOP AF Trial

Procedure sequence by quartiles

OR = 1.13 (1.06 - 1.20)

Short Learning Curve

No impact on adverse events or safety outcomes

Acute Procedural Success

A. Acute Procedural Success - by Patient

- 28 + 23 mm + focal
- 28 mm + focal
- Single 28 mm
- STOP AF 28 + 23 mm + focal

High Acute Success Rates

Andrade et al., Heart Rhythm 2011 8: 1444-51
The First-Generation Cryoballoon - Complications

<table>
<thead>
<tr>
<th>Outcome</th>
<th>n/N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phrenic Nerve Palsy (PNP)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any reported PNP</td>
<td>86/1349</td>
<td>6.38%</td>
</tr>
<tr>
<td>PNP persisting post procedure</td>
<td>67/1349</td>
<td>4.73%</td>
</tr>
<tr>
<td>PNP persisting &gt; 1 year</td>
<td>5/1349</td>
<td>0.37%</td>
</tr>
<tr>
<td>Pulmonary Vein Stenosis (PVS)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any PVS (per patient)</td>
<td>7/773</td>
<td>0.90%*</td>
</tr>
<tr>
<td>PVS requiring intervention</td>
<td>2/1163</td>
<td>0.17%</td>
</tr>
<tr>
<td>Vascular access complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding req. transfusion</td>
<td>3/1231</td>
<td>0.41%</td>
</tr>
<tr>
<td>Femoral artery pseudoaneurysm</td>
<td>4/1231</td>
<td>0.32%</td>
</tr>
<tr>
<td>Subclavian vein rupture</td>
<td>1/1231</td>
<td>0.08%</td>
</tr>
<tr>
<td>Periprocedure events</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td>4/1241</td>
<td>0.32%</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>3/1231</td>
<td>0.24%†</td>
</tr>
<tr>
<td>LA-esophageal fistula</td>
<td>0/1298</td>
<td>0.00%</td>
</tr>
<tr>
<td>Esophageal ulceration</td>
<td>6/116</td>
<td>5.17%‡</td>
</tr>
<tr>
<td>Pericardial effusion or tamponade</td>
<td>18/1231</td>
<td>1.46%</td>
</tr>
<tr>
<td>Cardiac tamponade</td>
<td>7/1231</td>
<td>0.57%</td>
</tr>
<tr>
<td>Pulmonary artery rupture</td>
<td>1/1231</td>
<td>0.08%</td>
</tr>
</tbody>
</table>

Reasonable Safety Profile

Andrade et al., Heart Rhythm 2011: 8 1444-51
Paroxysmal AF—Median Follow-up 30 months

Moderate Longterm Single-Procedure Success!

61.6% 76.9%

554 pts.

Median follow up 384 days
Group 1: 52% SR (1 bonus-freeze)
Group 2: 57% SR (2 bonus-freezes)

More Energy Does Not Improve Clinical Outcome!
The First-Generation Cryoballoon - Limitations

High Rate of PV-Reconduction

A Fürnkranz, KH Kuck, Heart Rhythm 2010;7(2):184-190
The Second-Generation Cryoballoon

More Homogeneous Cooling
28mm Balloon - Thermocouple Gel Model Isotherms Progression of Temperature Change at 20mm Depth By Minute

4 minutes on Artic Front® was roughly equivalent to 2-3 minutes with Arctic Front Advance™ as observed in the thermocouple gel model.

Medtronic data on file
## The Second-Generation Cryoballoon – Preclinical Data

<table>
<thead>
<tr>
<th>Dose</th>
<th>Balloon size</th>
<th>PVs treated</th>
<th>Species</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1x4min</td>
<td>23mm 28mm</td>
<td>20</td>
<td>Canine</td>
<td>Lesion circumferentiality improved with Arctic Front Advance vs. Arctic Front (100% of veins circumferentially transmural vs. 60%)</td>
</tr>
<tr>
<td></td>
<td>AF vs. AFA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1x2min vs.</td>
<td>23mm AFA</td>
<td>59</td>
<td>Canine</td>
<td>Both doses similar for circumferentiality and transmurality</td>
</tr>
<tr>
<td>1x4min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2x2min vs.</td>
<td>28mm AFA</td>
<td>17</td>
<td>Canine</td>
<td>Both doses similar for circumferentiality and transmurality; some lesion overlap</td>
</tr>
<tr>
<td>2x4min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2x2min vs.</td>
<td>28mm AFA</td>
<td>18</td>
<td>Porcine</td>
<td>Two of nine pulmonary veins with 2x2min reconnected at 30 days. All pulmonary veins with 2x4min isolated and circumferential lesions</td>
</tr>
<tr>
<td>2x4min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3. Medtronic data on file
1\textsuperscript{st} versus 2\textsuperscript{nd} Generation Cryoballoon

Shorter Freeze-Thaw Cycles

- 2 TP: CryoFlex, Lasso
- 1\textsuperscript{st} generation 28 mm cryoballon delivered over the wire to obtain LA-PV junction (antral) lesion
- PV occlusion angiography
- Cryoablation time: \textit{300} s; „bonus“-freeze

- 2 TP: CryoFlex, Lasso
- 2\textsuperscript{nd} generation 28 mm cryoballon delivered over spiral mapping and guiding catheter to obtain LA-PV junction (antral) lesion
- PV occlusion angiography
- Cryoablation time: \textit{240} s; „bonus“-freeze
<table>
<thead>
<tr>
<th>Catheter</th>
<th>No. Procedures</th>
<th>No. of Injections</th>
<th>COOLING RATE: MEAN TIME TO -30°C [s]</th>
<th>StDev</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AF</td>
<td>182</td>
<td>1789</td>
<td>48.7</td>
<td>25.4</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>AFA</td>
<td>43</td>
<td>409</td>
<td>40.3</td>
<td>14.8</td>
<td></td>
</tr>
</tbody>
</table>

Mean time to -30°C for AF Advance is detectably faster than AF by 8.4s (P<0.001)
Less variability observed (lower StDev).

<table>
<thead>
<tr>
<th>Catheter</th>
<th>No. Procedures</th>
<th>No. of Injections</th>
<th>MEAN MIN. ABLATION TEMP [°C]</th>
<th>StDev</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AF</td>
<td>182</td>
<td>1835</td>
<td>-44.33</td>
<td>7.82</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>AFA</td>
<td>43</td>
<td>419</td>
<td>-47.96</td>
<td>8.43</td>
<td></td>
</tr>
</tbody>
</table>

Mean minimum ablation temperature for AF Advance is detectably colder than AF by 3.6°C (P<0.001)
20.2% of AF Advance minimum temperatures were colder than -55°C (95% CI: 17.2%, 23.5%)
<table>
<thead>
<tr>
<th>Catheter</th>
<th>No. of Procedures</th>
<th>No. of Injections</th>
<th>MEAN THAW TIME TO +20°C [s]</th>
<th>StDev</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>AF</td>
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<td>1837</td>
<td>42.2</td>
<td>24.1</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>AFA</td>
<td>43</td>
<td>419</td>
<td>51.1</td>
<td>25.0</td>
<td></td>
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</tbody>
</table>

Mean thaw time for AF Advance increased by 9 s compared to AF (P<0.001).

Data St. Georg/Hamburg
### Minimum Ablation Temperature per Vein

<table>
<thead>
<tr>
<th>Catheter</th>
<th>No. of Injections/PVs</th>
<th>Mean Min. Ablation Temp [°C]</th>
<th>Delta [°C]</th>
<th>StDev [°C]</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LSPV</td>
<td>AF</td>
<td>36</td>
<td>-46.5</td>
<td>2.441</td>
<td>5.65</td>
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<tr>
<td></td>
<td>AFA</td>
<td>16</td>
<td>-49.2</td>
<td>7.18</td>
<td></td>
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<tr>
<td>LIPV</td>
<td>AF</td>
<td>16</td>
<td>-48.9</td>
<td>4.47</td>
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<tr>
<td></td>
<td>AFA</td>
<td>16</td>
<td>-51.7</td>
<td>6.76</td>
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<td>RSPV</td>
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<td>5.731</td>
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<td></td>
<td>AFA</td>
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<td>-52.4</td>
<td>5.83</td>
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<tr>
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<td>AF</td>
<td>45</td>
<td>-44.0</td>
<td>3.601</td>
<td>5.02</td>
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<td></td>
<td>AFA</td>
<td>16</td>
<td>-47.6</td>
<td>5.91</td>
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</tbody>
</table>

1= AF Advance always colder than AF

Data set from the vein size measurement study, all injections resulted in electrical isolation of PV.

Lower Balloon Temperatures

Data St. Georg/Hamburg
### Number of Ablations per Case

<table>
<thead>
<tr>
<th>Catheter</th>
<th>No. of Procedures</th>
<th>MEAN NO. OF ABLATIONS PER CASE</th>
<th>StDev</th>
<th>P-value</th>
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<tr>
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<td>10.09</td>
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<tr>
<td>AFA</td>
<td>43</td>
<td>8.81</td>
<td>1.28</td>
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</table>

Less variability in total number of ablations from case to case (lower StDev, see tight trend of Figure).

Data St. Georg/Hamburg
## Live Verification of PVI

<table>
<thead>
<tr>
<th></th>
<th>1st Generation CB</th>
<th>2nd Generation CB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live PVI verification</td>
<td>47%</td>
<td>76%</td>
</tr>
<tr>
<td>Time to isolation</td>
<td>59 ± 25 sec</td>
<td>52 ± 36 sec</td>
</tr>
</tbody>
</table>

1-Chierchia et al. Europace 2012;14,962-7
2-Fürnkranz et al., JCE 2013;24:492-497.
• 115 patients (42 female)
• Mean age 61 ± 11 years
• LA-diameter 43 ± 6 mm
• 93/115 (81%) paroxysmal AF, 22/115 (19%) short-lasting persistent AF
• No previous left atrial ablation
First Clinical Results – St. Georg/Hamburg

Acute Isolation in 445/448 (99%) PVs using the Single Big Cryoballoon advance (28mm)

<table>
<thead>
<tr>
<th></th>
<th>RSPV</th>
<th>RIPV</th>
<th>LSPV</th>
<th>LIPV</th>
<th>LCPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iso after 1. Appl., n (%)</td>
<td>100/1 (87)</td>
<td>88/1 (77)</td>
<td>82/1 (80)</td>
<td>98/1 (95)</td>
<td>7/1 (58)</td>
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<tr>
<td>Mean no. of Appl. Until compl. PVI</td>
<td>1.2±0.5</td>
<td>1.3±0.7</td>
<td>1.3±0.5</td>
<td>1.0±0.2</td>
<td>1.5±0.7</td>
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</tbody>
</table>

**Improved Acute Efficacy!**

Median Procedure Time: 127±32 min*

Median Fluoroscopy Time: 22±8 min*

* incl. 30min waiting period
Experience at St. Georg/Hamburg:

- Phrenic nerve palsy (PNP) in 4/115 (3.5%) patients during ablation of a RSPV (only 28mm CB)
- 1 PNP recovered after 10 months
- 3 PNPs persistent

Metzner, Kuck et al.; accepted for publication Journal of Cardiovasc Electrophysiol 12/2013
Cryoballoon-based PVI

- Over-the-wire system
- Single-shot device
- Electrical information from PV via central spiral catheter
Arctic Front Advance

Further improves Arctic Front by providing:

- More uniform cooling
- More distal, more homogeneous cooling
<table>
<thead>
<tr>
<th>Injection ports</th>
<th>Arctic Front</th>
<th>Arctic Front Advance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4</td>
<td>8</td>
</tr>
</tbody>
</table>
Variable PV Diameter

Arctic Front

Arctic Front Advance
Non-coaxial Alignment

courtesy of Dr. Vogt, Herzzentrum NRW, Bad Oeynhausen
Asklepios Klinik St Georg Procedure Metrics Compared to MDT Console Analysis

<table>
<thead>
<tr>
<th>Catheter</th>
<th>No of Injections</th>
<th>Cooling Rate: Mean Time to -30C (s)</th>
<th>St Dev</th>
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<table>
<thead>
<tr>
<th>Catheter</th>
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<th>Mean Min: Ablation (°C)</th>
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<td>7.82</td>
<td>P&lt;0.001</td>
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<table>
<thead>
<tr>
<th>Catheter</th>
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<th>Balloon Thaw Time to 20C</th>
<th>St Dev</th>
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<tr>
<td>AF</td>
<td>1021</td>
<td>34.1</td>
<td>16.4</td>
<td>P&lt;0.001</td>
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<tr>
<td>AFA</td>
<td>1523</td>
<td>49.2</td>
<td>26.4</td>
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</table>

Note: All data reflects 28mm balloon only
The Hamburg Experience

- n = 52 patients (20 female)
- Age 61±11 years
- 38 patients PAF, 14 patients persistent AF
- LA-diameter 42±8 mm
- Mean AF-duration 38 months (2 – 144 months)
- Art. HTN 37/52 (71%) patients
# Acute Procedure Success - Hamburg

## Acute Isolation in 200/200 PVs using the Single Big Cryoballoon (28mm)

<table>
<thead>
<tr>
<th></th>
<th>RSPV</th>
<th>RIPV</th>
<th>LSPV</th>
<th>LIPV</th>
<th>LCPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iso after 1. Appl., n (%)</td>
<td>47/52 (90)</td>
<td>43/52 (83)</td>
<td>38/44 (86)</td>
<td>43/44 (98)</td>
<td>4/8 (50)</td>
</tr>
<tr>
<td>Mean no. of Appl. Until compl. PVI</td>
<td>1.1</td>
<td>1.3</td>
<td>1.1</td>
<td>1.0</td>
<td>1.5</td>
</tr>
</tbody>
</table>

**Mean Procedure Time:** 145 ± 27 min  
**Mean Fluoroscopy Time:** 27 ± 8 min
Complications

• Phrenic nerve palsy in 1/52 (2%) patients
• No pericardial effusion/tamponade
• No TIA/stroke
Longterm Follow-up St. Georg

- 40/49 (82%) in SR, mean FU 440±39 days
- 1/50 (2%) patients lost to FU

Improved Long-Term Clinical Success

Metzner, Kuck; data submitted
Longterm Follow-up St. Georg

- 41/50 (82%) in SR, median FU xx±xx days
- 1/50 (2%) patients lost to FU

**Improved Long-term Clinical Success**

- SR: 41
- AF Recurrence: 9

Metzner, Kuck; data submitted
Prospective, randomized, multinational, multicenter trial

16 sites, 8 countries with n=768 (one time enrollment increase from 572)

Randomized 1:1
Cryoablation
(PVI only) vs.
RF ablation
stratified at age
65 at ratio of 1:1

Index Therapy

RF ablation
(PVI plus
additional lesions
if desired)

3-Month Blanking Period
• Cardiovers.
• Re-ablation
allowed

F/U visits & 24h Holter at months 3, 6, 9, 12, then every six months
• Max. F/U = 33 months
• Weekly Tele-ECG

Key Inclusion Criteria*
• Symptomatic paroxysmal atrial fibrillation (PAF) with ≥ 2 episodes
• Treatment failure of ≥ 1 AAD

Key Exclusion Criteria
• LA diameter > 55 mm
• EF < 35%
• ≥2 cardioversions within 2 years
• Any previous LA ablation or surgery
• Recent cardiac surgery or PCI, MI

Current Studies: FIRE & ICE Trial

Key Inclusion Criteria
• Symptomatic paroxysmal atrial fibrillation with ≥ 2 episodes
• Treatment failure of ≥ 1 AAD

Randomized 1:1
Cryoballoon ablation
vs
RF ablation
n=572

436/572 Patients Included

Key Exclusion Criteria
• LA diameter > 55 mm
• EF < 35%
• ≥2 cardioversions within 2 years
• Any previous LA ablation or surgery
• Recent cardiac surgery or PCI, MI

Follow-up visits at month 3, 6 and 12; Follow up call at month 9; Weekly Tele-ECG

Primary Outcome Parameter
Time to first documented recurrence of atrial arrhythmias or prescription of AAD or re-ablation, whatever comes first
Future Studies: Individualized Ablation Strategy

Patients with PAF Randomized 1:1

Standard Freeze Cycle 240 sec.

Individualized Ablation: Time-to-Effect + 60/90/120 sec.

Clinical Follow-up
**FIRE AND ICE Trial Design and Enrollment**

**Key Inclusion Criteria**
- Symptomatic paroxysmal atrial fibrillation (PAF) with ≥ 2 episodes
- Treatment failure of ≥ 1 AAD

**Randomized 1:1**
- Cryoballoon ablation
  - n=286
- RF ablation
  - n=286

**Index Therapy**

**3 month Blanking Period**
- No cardioversions
- Re-ablation for enhancement

**Follow-up visits at month 3, 6 and 12; Follow up call at month 9; Weekly Tele-ECG**

**Key Exclusion Criteria**
- LA diameter > 55 mm
- EF < 35%
- ≥2 cardioversions within 2 years
- Any previous LA ablation or surgery
- Recent cardiac surgery or PCI, MI
### Principal Investigators and Steering Committee

#### Principal Investigator
- Prof. Dr. Karl-Heinz Kuck, Hamburg, Germany

#### Co-chair
- Prof. Dr. Josep Brugada, Barcelona, Spain

#### Steering Committee Members
- Dr. Jean-Paul Albenque, Toulouse, France
- Prof. Dr. Josep Brugada, Barcelona, Spain
- Dr. David Wyn Davies, London, UK
- Prof. Dr. Karl-Heinz Kuck, Hamburg, Germany
- Prof. Dr. Claudio Tondo, Milan, Italy

#### Current Participating Countries (# of Sites)
- Belgium (2)
- Czech Republic (1)
- France (5)
- Germany (4)
- Hungary (1)
- Italy (2)
- Netherlands (1)
- Spain (4)
- Switzerland (1)
- UK (1)
Catheter ablation of atrial fibrillation

Agenda

• Role of PV’s as site of trigger of AF
• Durable PVI
  – Contact force
  – Laser
  – Cryo
• Mechanisms to maintain AF in persistent/longstanding persistent AF
  – Rotors
Mechanisms of atrial fibrillation

Calkins et al, Atrial fibrillation; Catheter ablation; Surgical ablation, Heart Rhythm 2012;9:632–696
Follow up: 49.5 (Q1, Q3; 35.7; 61.2) month
Sinus Rhythm in 45.0%

Tilz, Ouyang et al., JACC 2012
Primary Outcome

Documented AF > 30 seconds after one procedure with or without AAD

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>81</th>
<th>60</th>
<th>60</th>
<th>41</th>
<th>36</th>
<th>23</th>
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<tbody>
<tr>
<td>Pulmonary vein isolation</td>
<td></td>
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<td></td>
<td></td>
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<td></td>
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<tr>
<td>Isolation + Electrograms</td>
<td>244</td>
<td>242</td>
<td>161</td>
<td>137</td>
<td>124</td>
<td>72</td>
</tr>
<tr>
<td>Isolation + Lines</td>
<td>244</td>
<td>240</td>
<td>152</td>
<td>133</td>
<td>115</td>
<td>57</td>
</tr>
</tbody>
</table>

p=0.15
Anatomically: Extension of Myocardial sleeve into all PVs: 1-3 cm
Histological basis: The presence of P, transitional and Purkinje cell and Discrete Inon channel (Iki)
Clinical EP finding:
  - Short ERP and slow conduction
  - Spontaneous or induced PV tachycardia within isolated PVs (6-45%)
2: Ablation Techniques

1: Complete electrical isolation
Waiting time >20 min

2: Conduction block
if linear lesion

2012 HRS/EHRA/ECAS: CA and SA of AF
Case 1

Figure 2. A and B. Tracings are ECG leads I, aVF, and V1 and intracardiac electrograms recorded from 2 Lasso catheters within the RSPV and RIPV and a catheter inside the CS before and after complete isolation of the right-sided PVs in a patient with persistent AF for 14 days. In A, note before ablation (1) regular PV activity recorded within the RSPV with stable CL of 130 ms and (2) disorganized activation within the RIPV and the LA recorded from the CS with variable CL. In B, note (1) sinus rhythm after AF termination and continuous PV tachycardia within the RSPV with a CL of 120 ms and (2) passive organized activation with Wenckebach conduction from the RSPV into the RIPV.
CPVI in patients with short persistent AF

40 pts with persistent AF

After the right CCLs

SR in 3 pts
Macro-AT in 4 pts
AFL 3
LAMRT 1

AF in 33 pts

After the left CCLs

AF in 18 pts
Macro-AT in 6 pts
SR in 9 pts

AFL 1
LAMRT 5

AF duration
- 7 days - 1 months in 10 pts
- one - 3 months in 11 pts
- 3 - 6 months in 12 pts
- 6 - 16 months in 7 pts

90% during FU after 2nd procedure

Ouyang et al. Circulation 2005
1) „Fractionated electrograms composed of 2 deflections or more, and/or pertubation of the baseline with continuous deflections“
For example posterior LA septum:

2) „atrial electrograms with a very short CL (≤120ms)“
For example LA roof:

3) „CFAES usually are low-voltage multiple potential signals between 0.06 and 0.25 mV“

Haissaguerre et al. JCE 2005
Nademane K et al, JACC 2004;43:1044-2053
Definition of CFAES (10 sec recording period)

1) „Fractionated electrograms composed of 2 deflections or more, and/or pertubation of the baseline with continuous deflections“
For example posterior LA septum:

2) „atrial electrograms with a very short CL (≤120ms)“
For example LA roof:

3) „CFAES usually are low-voltage multiple potential signals between 0.06 and 0.25 mV“

Haissaguerre et al. JCE 2005
Nademanee K et al, JACC 2004;43:1044-2053
Suggested Mechanisms underlying CFAE

• Pathological anisotropic conduction and focal micro-reentry (Gardner & Witt 1985, Allesie MA)

• **Slow conduction and pivot points** of the wavelets (Konning & Allesie 1996)

• Calcium-transient triggering activities from hyperactive **autonomic plexi** (Scherlag, Nakagawa, Po, Jackman 2004)

• Border zone of **mother rotors** (Jalife et al)

→ CFAEs represent areas that perpetuate AF
Complex fractionated EG were mainly found in 4 atrial regions

1) Septum + Bachman  
2) Left postsept MA + CS os  
3) PV  
4) LA roof  
5) MA  
6) Cavo-tricuspid Isthmus  
7) Crista terminalis  
8) RAA and LAA  
9) SVC-RA junction
Clinical trials on PVI versus PVI + CFAE

<table>
<thead>
<tr>
<th>Study</th>
<th>Publication Year</th>
<th>N</th>
<th>Age (year)</th>
<th>LA size (mm)</th>
<th>AF duration (year)</th>
<th>Study design</th>
<th>Follow-up (month)</th>
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<tr>
<td>Baise</td>
<td>2009</td>
<td>35</td>
<td>34</td>
<td>57=8.1</td>
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<td>Verma-1A</td>
<td>2007</td>
<td>60</td>
<td>60</td>
<td>57=12</td>
<td>56±9</td>
<td>42±9</td>
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<td>Verma-1B</td>
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<td>40</td>
<td>40</td>
<td>57=12</td>
<td>56±9</td>
<td>42±9</td>
<td>43±1</td>
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<td>Oral</td>
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<td>57=10.6</td>
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<td>47±6</td>
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<td>49</td>
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<td>45±1.6</td>
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<td>Verma-2</td>
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<td>60=11</td>
<td>51±19</td>
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<td>Verma-3A</td>
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<td>43±5</td>
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<td>Verma-3B</td>
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<td>12</td>
<td>55=11</td>
<td>59±10</td>
<td>43±5</td>
<td>41±6</td>
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</table>

*Verma-1A: Study of paroxysmal AF; *Verma-1B: Study of nonparoxysmal AF; *Verma-3A: Study of paroxysmal AF; Verma-3B: Study of nonparoxysmal AF; P: pulmonary vein antrum isolation; CFAE: complex fractionated atrial electrogram; LA: left atrium; AF: atrial fibrillation; RCT: randomized controlled trial; MC: matched controlled study.
Clinical trials on PVI + CFAE versus PVI

Li WJ and Ma CS. Circ Arrhythms Electrophsiol 2011 in Press
Case 2: persistent AF of 6 months

LA Fragmented P

Only 5 RF application in LA anterior and anteroseptal area
AF to common-type AFL after ablating fragmented potentials
Hypothesis: Stable Sources Perpetuate AF

- Optically Mapped Sheep atria \(^1,2\)
- Sometimes stable, often migratory \(^1,2\)

In human AF:
- Little or no direct evidence for rotors \(^1\text{-}^5\)

If Stable, Attractive Sites For Localized Ablation

Rotor Mapping Systems

Topera  Carto Finder  EP Solution  Cardio Insight
RA Rotor with LA activation
LA Rotor with passive activation of RA
### Summary Results: Acute Endpoint

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Conventional</th>
<th>FIRM-Guided</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. Pts with Sustained AF</td>
<td>63</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>No. with Rotors/Foci, n/%</td>
<td>61 (97%)</td>
<td>32 (100%)</td>
<td>0.31</td>
</tr>
<tr>
<td>No. Sources / patient</td>
<td>1.9±0.8</td>
<td>2.1±0.8</td>
<td>0.28</td>
</tr>
</tbody>
</table>

* (1) Phrenic nerve capture; (2) at pacing lead
CONFIRM Trial: Long-Term Single Procedure Efficacy

FIRM-Guided, 84.3%
(84% had Implanted Monitors)

Conventional, 50.5%
(23% had Implanted Monitors)

P=0.04
Freedom from AF based on whether the procedure directly or coincidentally ablated rotors or focal sources (green) or missed rotors/sources (blue)
### Topera Ablation at St. Georg Hospital

<table>
<thead>
<tr>
<th>Patients Number</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous AF</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>Total number of rotors</td>
<td>3±1,6</td>
</tr>
<tr>
<td>Number of rotors right atrium</td>
<td>0,5±0,7</td>
</tr>
<tr>
<td>AF termination during ablation</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>CL increase &gt; 10%</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>Firm ablation time</td>
<td>15±9 min</td>
</tr>
<tr>
<td>Pulmonary vein isolation</td>
<td>20 (100%)</td>
</tr>
<tr>
<td>CTI ablation</td>
<td>9 (45%)</td>
</tr>
<tr>
<td>Mitral isthmus line</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>Anterior line</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>Roof line</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Clinical outcome</td>
<td>Without blanking period</td>
</tr>
<tr>
<td></td>
<td>–SR in 70% (n=14)</td>
</tr>
</tbody>
</table>
Single procedure success

15/25 patients (60%) in SR during 13 ± 1 months FU
20/25 patients without AF recurrence
Outcome during 13±1 months FU

• Single procedure success
  – SR in 15/25 (60%) patients
  – Clinical arrhythmia: PAF in 4 pts (16%), pers. AF in 1 pts (4%), AT/Aflu in 5 pts (20%)

• Multiple procedure success (including 3 months blanking periode)
  – Redo in 6 patients with ATa recurrence
  – SR in 20/25 (80%) patients
Multiple procedure success

20/25 patients (80%) in SR during 13 ± 1 months FU
NONINVASIVE EP IMAGING
EP Solutions

MRI or CT SCAN

ECG REGISTRATION

TORSO AND HEART VOLUME RECONSTRUCTION

VOLTAGE, ISOCHRONE AND PHASE MAPS OF EPICARD AND ENDOCARD
The System – EP Solutions
Noninvasive ECG Imaging

Noninvasive ECGI uses numerical reconstruction and visualization of the electrical heart activity based on the ECG data measured on the body surface.
EP Solutions Non-invasive Mapping System

3D modeling

ECG preprocessing

Numerical calculation

Visualization
Clinical Applications

VENTRICULAR TOPICAL DIAGNOSTICS

WPW DIAGNOSTICS

ATRIAL TOPICAL DIAGNOSTICS

ATRIAL FLUTTER AND FIBRILLATION

CRT RESPONSE AND OPTIMIZATION
MAPPING DURING AF
Patient: S.H. Date: 13.03.2013
Rotor migrating around ICV and LIPV. Isopotential phase map

Patient: S.K-P. Date: 19.04.2013

Time range: 600 ms
• Purpose of the study –
• To assess whether the mathematical model to identify rotors using the EP Solution noninvasive body-surface mapping system can be confirmed by Pentaray recordings from the core of the rotor
# Baseline Patient Characteristics: Pentaray Study

<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>51</td>
<td>71</td>
<td>45</td>
<td>70</td>
<td>55</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>male</td>
<td>female</td>
<td>male</td>
<td>male</td>
<td>male</td>
</tr>
<tr>
<td><strong>Type of AF</strong></td>
<td>persistent</td>
<td>persistent</td>
<td>persistent</td>
<td>persistent</td>
<td>persistent</td>
</tr>
<tr>
<td><strong>LA Diameter (mm)</strong></td>
<td>46</td>
<td>50</td>
<td>44</td>
<td>45</td>
<td>46</td>
</tr>
<tr>
<td><strong>LVEF (%)</strong></td>
<td>&gt;55</td>
<td>&gt;55</td>
<td>&gt;55</td>
<td>&gt;55</td>
<td>&gt;55</td>
</tr>
<tr>
<td><strong>CHADS2-VASC Score</strong></td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Patient 1</td>
<td>Patient 2</td>
<td>Patient 3</td>
<td>Patient 4</td>
<td>Patient 5</td>
</tr>
<tr>
<td>------------------</td>
<td>-----------</td>
<td>-----------</td>
<td>-----------</td>
<td>-----------</td>
<td>-----------</td>
</tr>
<tr>
<td>Procedure time (min)</td>
<td>160</td>
<td>280</td>
<td>180</td>
<td>185</td>
<td>150</td>
</tr>
<tr>
<td>Fluoro time (min)</td>
<td>20</td>
<td>34</td>
<td>21</td>
<td>18</td>
<td>10</td>
</tr>
<tr>
<td>Rotor location</td>
<td>Septal anterior LA</td>
<td>No stable rotor</td>
<td>Pentaray only</td>
<td>Pentaray only</td>
<td>RSPV, LSPV, LA roof</td>
</tr>
</tbody>
</table>
Patient 4: Standard ECG Leads

I
II
III
AVF
AVL
AVR

Patient 4
Pentaray Unipolar EGMs

80% EGMs within LA demonstrate fractionation

challenging to identify any type of organized activity

20% EGMs are more regular

possible to identify organized activity

Patient 4
LA Carto Map

Site of analysis

Patient 4
Bipolar Voltage Map

Patient 4
Phase Map Analysis

3D Pentaray LA map

2D phase map based on Pentaray data

Patient 4
No stable rotor identified without filtering
Filter setting: Range 3 - 7 Hz

Filtering range of 3 - 7 Hz facilitates visualization of stable rotors

video: 0 -- 200 ms

50 ms  110 ms  150 ms  Patient 4
Pentaray EGMs

Patient 4
Patient 5: Standard ECG Leads

I

II

III

aVF

aVL

aVR
Pentaray Unipolar EGMs

70% EGMs within LA demonstrate fractionation challenging to identify any type of organized activity

30% EGMs are more regular possible to identify organized activity

Patient 5
AMYCARD PHASE MAPPING

- Body surface mapping
- Reconstruction of the Heart unipolar EGMs
- Unipolar EGMs → Phase maps
- Analysis of 7-10 atrial EGM fragments between QRS
- Identify and visualize organized activity
Bipolar Voltage Map

Patient 5
NONINVASIVE PHASE MAPPING

Baseline map:
Stable rotors in LSPV and RSPV

Patient 5
Baseline map:
LSPV: during long Pentaray recording (15 s), 200ms fragment with rotor in stable location. Other fragments do not demonstrate stable rotor

Filtration range 3 – 7 Hz

Patient 5
PENTARY PHASE MAPPING

Baseline recordings

1  2

5  6
Baseline map:
RSPV: during long Pentaray recording (15 s), 180ms fragment with stable rotor in place. Other fragments do not demonstrate stable rotor
PENTARY PHASE MAPPING

Step 1: Before PVI
Following isolation of RSPV
Stable rotor only in LSPV, no rotor in RSPV
Following isolation of LSPV and RSPV:
Stable rotor at LA roof
Following isolation of LSPV and RSPV:
Stable rotor at LA roof
During long recording using Pentaray (15 s), two 350ms fragments confirm rotor at same location.
Following isolation of LSPV and RSPV:
Stable rotor at LA roof
Following isolation of LSPV, RSPV and deployment of LA roof line: Rotor not at stable location. Rotor core drifting along the LA roof line.
Conclusions

• The importance of rotors in maintaining AF in the human heart still unknown.
• Epi- or endocardial mapping or both?
• Rotors identified by phase mapping from the body surface can be modified/eliminated by linear ablation, but do not change/terminate AF in persistent AF
• More research is needed – threshold for the amount of fractionation and the amplitude of local EG’s still allowing a valid phase map
NONINVASIVE vs. PENTARAY

- Stability of the analysis strongly depends on EGs regularity/amplitude
- Pentaray EGs are more fractionated, noninvasive EGs are more smoothed
- Noninvasive EGs more frequently produce rotors, but pentary data also show rotors at the same places
The ccw rotor in LA

Isochrone map

Phase map

Patient: Date:
The ccw rotor in LA

Isochronal map

Phase map

Patient:  Date:
"Rotor criteria" at CARTO or EP STATION

The absence of a rotor

The presence of a rotor

Green circle - is a beginning of bipolar spike (activation time) at Pentaray poles.

Maximum difference between activation times >40 ms is a "Sign of a Rotor"
New signal processing mode

1. Initial signal

2. QRST recognition

3. Subtraction of the averaged QRST

4. Spectral filtration (3-7 Hz or 3-9 Hz)

Patient: E.G.  Date: 8.02.2013
Phase map during QRS

QRS N1

“false rotors from QRS??”

QRS N2

? Real rotors?

QRS subtraction

with QRS

QRS subtraction
Patient data

Name: BHJ
Gender: Male
Age: 74 y.o.
Diagnosis: Persistent atrial fibrillation
Date of the study: 28.10.2014
The patient with persistent Afib was examined.

Simultaneous electroanatomical mapping of LA using CARTO III MEM System with Pentaray catheter and noninvasive atrial mapping using Amycard System were performed. Phase maps based on unipolar electrograms recorded by Pentaray catheter and phase maps obtained by Amycard System were compared.
Noninvasive phase mapping results

Phase maps

Spatial distribution of rotor’s cores localization
CARTRO based LA 3D model

Red dots present pentaray catheter poles positions
Local electrograms obtained by pentaray catheter
Observation of the rotor, 0 ms

Noninvasive phase mapping

Phase mapping based on Pentaray catheter

Bipolar electrograms (CS+Pentaray)
Observation of the rotor, 30 ms

Noninvasive phase mapping

Phase mapping based on Pentaray catheter

Bipolar electrograms (CS+Pentaray)
Observation of the rotor, 60 ms

Noninvasive phase mapping

Bipolar electrograms (CS+Pentaray)

Phase mapping based on Pentaray catheter
Observation of the rotor, 90 ms

Noninvasive phase mapping

Phase mapping based on Pentaray catheter

Bipolar electrograms (CS+Pentaray)
Observation of the rotor, 120 ms

Noninvasive phase mapping

Phase mapping based on Pentaray catheter

Bipolar electrograms (CS+Pentaray)
Video of the rotor dynamics

Noninvasive phase mapping

[ video ]
Video of the rotor dynamics

Phase mapping based on CARTO recordings from pentaray catheter

[ video ]
Conclusions

1. Phase mapping based on pentaray catheter confirmed the presence of rotors (vortex waves) during AFib.
2. The locations of the rotor based on noninvasive phase mapping and based on pentaray catheter recordings was the same.
Conclusion

• GAPAF – complete PVI is associated with less AF recurrences, but with a 70% gap rate after 3 months
• Durable PVI – major future challenge
  – CF guided ablation improves clinical outcome
  – Cryo – single shot device, the new device:
    – High efficacy, short procedure duration, easy to use
• Mechanisms to sustain AF in persistent/longstanding persistent AF
  – Role of rotors – for maintenance of AF is an interesting concept,
  – It’s role as a potentially new treatment option beyond PVI needs further investigation
Conclusion

- During persistent AFib most of the unipolar EGs are fractionated
- It is not possible to reconstruct activation maps using common methods: dv/dt or maximum of bipolar EGs. But activation can be reconstructed using phase mapping.
- Phase mapping without filtration cannot identify clearly rotors, only multiple wavelets
- But phase mapping after filtration 3-7 Hz can reconstruct a rotor
ECG

Patient: S.K-P. Date: 19.04.2013
Rotor migrating around ICV and LIPV. Isopotential phase map
Patient: S.H. Date: 13.03.2013
Rotor migrating around RA appendage.
Isopotential phase map

Patient: S.H. Date: 13.03.2013

Time range: 500 ms
ECG fragment used in calculations – 820 ms

Patient: E.G.  Date: 8.02.2013
Rotor migrating in RA. Phase isopotential map

anatomical model

Patient: E.G.  Date: 8.02.2013
Rotor - evolution. Phase Isopotential Map

Patient: E.G.  Date: 8.02.2013
Rotor migrating around RA.
Isopotential phase map

Patient: E.G.  Date: 8.02.2013

Time range: 600 ms

[video]
Case №4 (Pt. D. 45 y., Pers. AF)
Case №1 (Pt. D. 45 y., LSP AF)
Case №1 (Pt. D. 45 y., LSP AF)
Noninvasive ECG Imaging

Noninvasive ECGI uses numerical reconstruction and visualization of the electrical heart activity based on the ECG data measured on the body surface.
EP Solutions Non-invasive Mapping System

3D modeling

ECG preprocessing

Numerical calculation

Visualization
Validating Accuracy

Validating Accuracy

Rotors in VT/VF

Objectives

• To assess whether a novel non-invasive mapping system can record and display rotors during VT/VF in humans
• To study the activation pattern during VT/VF
• To understand the mechanism that maintains VT/VF in humans
• To develop an ablative strategy to target rotors in patients with VT/VF based on information from non-invasive mapping
Phase mapping - Hilbert transform

Phase Mapping of Cardiac Fibrillation
K Umaphathy et al. Circ Arrhythm Electrophysiol. 2010; 3:10S-14
<table>
<thead>
<tr>
<th>Patient</th>
<th>Dz</th>
<th>Episodes</th>
<th>TCL (ms)</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pat N1, 51 male</td>
<td>ICM</td>
<td>MMVT</td>
<td>300</td>
<td>6 s, self-term</td>
</tr>
<tr>
<td>Pat N2, 54 male</td>
<td>Sarcoidosis</td>
<td>3 MMVT/PMVT</td>
<td>260/220/210/180</td>
<td>18 s, CV</td>
</tr>
<tr>
<td>Pat N3, 28 male</td>
<td>HCM</td>
<td>VF</td>
<td>200</td>
<td>12 s, self-term</td>
</tr>
<tr>
<td>Pat N4, 38 female</td>
<td>Brugada</td>
<td>VF</td>
<td>160</td>
<td>17 s, CV</td>
</tr>
<tr>
<td>Pat N5, 60 male</td>
<td>ICM</td>
<td>MMVT</td>
<td>450</td>
<td>25 s, ATP</td>
</tr>
<tr>
<td>Pat N6, 64 male</td>
<td>ICM</td>
<td>MMVT</td>
<td>390</td>
<td>27 s, ATP</td>
</tr>
<tr>
<td>Pat N7, 79 male</td>
<td>ICM</td>
<td>MMVT</td>
<td>460</td>
<td>sustained, self-term</td>
</tr>
<tr>
<td>Pat N8, 58 male</td>
<td>Myocarditis</td>
<td>VF/VT</td>
<td>160/265</td>
<td>10 s, CV/30 s, CV</td>
</tr>
</tbody>
</table>
Patient 2 - Sarcoidosis

54 yo male, non-sustained VT, syncope, EF 50%
transthoracic needle biopsy: sarcoidosis
MRI scars: IVS, RVOT, mid postero-lateral LV (epi)
Patient 2 - Sarcoidosis

1st MMVT 2 s

TCL 260 ms

PMVT 8 s

TCL 180 ms

2nd MMVT 6 s

TCL 220 ms

3rd MMVT 2 s

TCL 210 ms
1st MMVT

TCL 260 ms

2 s
TCL 220 ms

6 s

2nd MMVT
2nd MMVT

TCL 220 ms

6 s
3rd MMVT

TCL 220 ms

2 s
Patient 4 - Brugada Syndrome

38 yo female, syncope, EF 60%, Brugada syndrome verified by gene testing: 1233 del in exon 10 of SCN5A, positive Ajmaline test.

VF 17 s, TCL 160 ms.
Endo- and Epicardial Reconstruction of EGMs
Patient 4 - VF

TCL 160 ms

17 s
Patient 4 - VF

TCL 160 ms

17 s
Patient 7 - Ischemic VT

79 yo male, postero-lateral MI, CABG, EF 50%, VT CL 460 ms
CASE N7

79 y.o. male, Postero-lateral MI, CABG, PCI, Incessant VT, EF 50%

Courtesy of E. Wissner
Phase Modification of Unipolar EGs
Carto Propagation Map
Scar with Rotor at Entrance Site?
Patient 8 - Myocarditis

58 yo male, hx of myocarditis in the past, EF 60%, spontaneous VT necessitating CV, over-drive pacing induces VF CL 160 ms
Patient 8 - Myocarditis

Courtesy of E. Wissner
Limitations

• Small group – no statistical data
• Phase mapping is not validated in humans
• Low resolution of noninvasive ECGI system
Summary

Rotors in VF

• Noninvasive ECGI in patients with VF demonstrates that rotors and multiple wavelets can coexist

• Noninvasive ECGI in patients with VT demonstrates a stable rotor, but its relationship to the macroreentry circuit are unknown

• Additional studies are required to determine the effectiveness of noninvasive ECGI to guide invasive interventional treatment of ventricular arrhythmias