ASSERT Sub Study
Temporal relationship between Subclinical Atrial Fibrillation and Embolic Event

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• Atrial fibrillation (AF) increases the risk of stroke (Wolf PA, Stroke 1991)

• A significant proportion of AF is asymptomatic and may reveal itself only after stroke occurred (Ziegler P, Stroke 2010)

• Modern dual chamber pacemakers (PM) are able to document and quantify individual episodes of atrial tachyarrhythmias (AT) for prolonged periods of time

• Device-detected ATs correlate well with ECG documentation of AF (subclinal atrial fibrillation-SCAF) (Pollak WM, PACE 2001) and occur in over 40% of PM patients without previous history of AF (Healey JS, NEJM 2012)
## ASSERT TRIAL

<table>
<thead>
<tr>
<th>Event</th>
<th>SCAF (&gt;6min, &gt;190 bpm)</th>
<th>SCAF Detected vs. not detected</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not detected N= 2319</td>
<td>Detected N= 261</td>
</tr>
<tr>
<td></td>
<td>events</td>
<td>%/year</td>
</tr>
<tr>
<td>Ischemic Stroke or Systemic Embolism</td>
<td>40</td>
<td>0.69</td>
</tr>
<tr>
<td>Vascular Death</td>
<td>153</td>
<td>2.62</td>
</tr>
<tr>
<td>Stroke / MI / Vascular Death</td>
<td>206</td>
<td>3.53</td>
</tr>
<tr>
<td>Clinical Atrial Fibrillation or Flutter</td>
<td>71</td>
<td>1.22</td>
</tr>
</tbody>
</table>

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UNRESOLVED QUESTION

Are SCAF causally implicated in stroke or simply a marker of risk?

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PREVIOUS FINDINGS

Detection of atrial high-rate events by continuous Home Monitoring: clinical significance in the heart failure–cardiac resynchronization therapy population

Nesan Shanmugam¹, Annegret Boerdelein², Jochen Proff², Peter Ong¹, Oswaldo Valencia¹, Sebastian K.G. Maier³, Wolfgang R. Bauer³, Vince Paul⁴, and Stefan Sack⁵

- 560 CRT patients followed with REMOTE MONITORING for 370 days
- Stroke patients (n= 11)
- 27% of patients were in AT/AF at the time of the stroke
- 73% of patients did not show a temporal association of AT/AF and stroke

Stroke patients (n= 40)

- 20 pts with SCAF detected prior to the stroke
  - 30% was in SCAF at the time of the stroke
  - 70% did not show a temporal association SCAF and stroke (mean interval 168± 199 days earlier)
Understand the stroke mechanism among the ASSERT study population, by evaluating the Temporal Relationship between subclinical atrial fibrillation (SCAF) and ischemic stroke/systemic embolism.
METHODS

Patient Eligibility:
• Enrolled after new dual-chamber pacemaker or ICD
• Age ≥ 65 years
• History of hypertension
• Excluded if any history of AF
• Excluded if on Vitamin K antagonists

Device programmed according to protocol-specific setting:
• Atrial lead sensitivity (0.1-0.5 mV)

Threshold for SCAF episode detection was:
• Atrial rate >190 beats per minute
• Lasting > 6 minutes

Stored Device Data (Date, Time of onset and duration*) of all SCAF events detected for the entire FU
*For multiple SCAF events occurring in a single day, total duration was considered

Outcome
• Ischemic stroke or systemic embolism

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ASSERT Study Population (n=2580)

- Ischemic stroke or Systemic embolism before 3-month visit (n=8)
  - SCAF not detected (n=25)
  - SCAF detected (n=26)

- Ischemic stroke or Systemic embolism after 3-month visit (n=51)
## BASELINE CHARACTERISTICS

<table>
<thead>
<tr>
<th></th>
<th>SCAF not detected (n=25)</th>
<th>SCAF detected (n=26)</th>
<th>Overall (n=51)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age ~ years</strong>*</td>
<td>Mean (SD)</td>
<td>75.4 ± 6.7</td>
<td>80.3 ± 7.1</td>
</tr>
<tr>
<td>Male sex ~ no. (%)**</td>
<td></td>
<td>20 (80)</td>
<td>8 (31)</td>
</tr>
<tr>
<td>Ischemic Stroke ~ no. (%)</td>
<td></td>
<td>21 (84)</td>
<td>25 (96)</td>
</tr>
<tr>
<td>Systemic Embolism ~ no. (%)</td>
<td>N (%)</td>
<td>4 (16)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>CHADS2 score</td>
<td>Mean (SD)</td>
<td>2.8 ± 1.2</td>
<td>2.7 ± 1.1</td>
</tr>
<tr>
<td>CHA2DS2-VASc score</td>
<td>Mean (SD)</td>
<td>4.3 ± 1.4</td>
<td>4.7 ± 1.0</td>
</tr>
<tr>
<td>Risk factors for stroke ~ no. (%)</td>
<td></td>
<td>5 (20)</td>
<td>4 (15)</td>
</tr>
<tr>
<td>Prior stroke</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior TIA</td>
<td>4 (16)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of HF</td>
<td>2 (8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>9 (36)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior MI</td>
<td>6 (24)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sinus node disease w or w/o AV node disease ~ no. (%)</td>
<td>11 (44)</td>
<td>12 (46)</td>
<td>23 (45)</td>
</tr>
<tr>
<td>Aspirin ~ no. (%)</td>
<td>13 (52)</td>
<td>15 (58)</td>
<td>28 (55)</td>
</tr>
<tr>
<td><strong>Time from Device Implant to Stroke (days)</strong></td>
<td>Mean (SD)</td>
<td>580 ± 357</td>
<td>703 ± 394</td>
</tr>
<tr>
<td><strong>Time from Stroke to last follow up (days)</strong></td>
<td>Mean (SD)</td>
<td>477 ± 399</td>
<td>452 ± 480</td>
</tr>
<tr>
<td><strong>Time from Device Implant to Stroke (days)</strong></td>
<td>Median (P25-P75)</td>
<td>570 (263-816)</td>
<td>670 (456-900)</td>
</tr>
<tr>
<td><strong>Time from Stroke to last follow up (days)</strong></td>
<td>Median (P25-P75)</td>
<td>404 (93-866)</td>
<td>350 (41-731)</td>
</tr>
</tbody>
</table>
STUDY FLOW CHART

SCAF detected (n=26)

- SCAF within 1 year before or after Stroke occurred (n=18)
- SCAF more than 1 year before or after Stroke occurred (n=8)

- > 1 year AFTER Stroke (n=1)
- > 1 year BEFORE Stroke (n=7)
Results: SCAF occurring within 1 year before or after Stroke

SCAF detected > 30 days BEFORE the Stroke

SCAF detected < 30 days BEFORE the Stroke

SCAF detected AFTER Stroke
Results: SCAF occurring PRIOR to the Stroke

- **In 14 PATIENTS (27%) SCAF occurred > 30 days prior to the STROKE**
  - The most recent episode of SCAF
  - -> median interval of 339 days (P25-P75:211-619 days) before
  - -> median duration of 4.2 hours (P25-P75:0.80-466 hours)

- **In ONLY 4 PATIENTS (8%) SCAF occurred within 30 days prior to the STROKE**
  - 8# had last SCAF 11 days before (6 minutes)
  - 9# had SCAF at the time of his stroke (2.7 hours)
  - 10# had last SCAF 9 days before (4 days)
  - 11# had last SCAF 15 days before (12 hours)
Results: SCAF occurring AFTER the Stroke

• In 8 patients (16%), SCAF s were detected only AFTER the stroke at a median interval of 101 days (P25-P75:14-196).

• The maximum median SCAF duration on a single day was 6.3 hours (P25-P75:1.9-10.3).
CONCLUSIONS I

TRENDS SUBSTUDY

40 stroke patients:

- 20 pts with AT/AF detected prior to the embolic events
  - 45% pts with no AT/AF within 30 days of stroke
  - 15% pts with AT/AF within 30 days
  - 30% pts was in AT/AF at the time of their stroke
  - 55% with diagnosis of AF prior to the enrolment

→ INDIRECT MECHANISM OF STROKE?
→ SCAF AS A RISK MARKER?

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### CONCLUSIONS II

<table>
<thead>
<tr>
<th>Study</th>
<th>Groups</th>
<th>N</th>
<th>Onset of Monitoring after stroke (days)</th>
<th>Duration of monitoring (days)</th>
<th>Proportion with AF (%)</th>
<th>Use of oral anticoagulant (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EMBRACE</strong> (NEMJ 2014)</td>
<td>Usual*</td>
<td>285</td>
<td>75.1±38.6</td>
<td>90</td>
<td>3.2</td>
<td>11.1</td>
</tr>
<tr>
<td></td>
<td>Intensive°</td>
<td>286</td>
<td></td>
<td></td>
<td>16.1</td>
<td>18.6</td>
</tr>
<tr>
<td><strong>CRYSTAL AF</strong> (NEMJ 2014)</td>
<td>Usual*</td>
<td>220</td>
<td>38.1±27.6</td>
<td>180</td>
<td>1.4</td>
<td>4.6</td>
</tr>
<tr>
<td></td>
<td>Intensive§</td>
<td>221</td>
<td></td>
<td></td>
<td>8.9</td>
<td>10.1</td>
</tr>
</tbody>
</table>

*12-lead ECG and Holter ECG monitoring for 24-48 h. ° Continuous surface ECG for 4 weeks. §Subcutaneous ECG monitoring with an implanted device for up to 3 years.

Modified from Camm J, 2014

--> SCAF AFTER CRYPTOGENETIC STROKE STILL THE CAUSE OF THE EMBOLIC EVENT?
THANK YOU FOR YOUR ATTENTION