Panoramic Mapping of AF: Toys or Useful Tools?

Dr Ross Hunter
Barts Heart Centre
HRC 2018
PVI perhaps as good as anything currently....

But PVI not enough for many!

(Verma et al, NEJM 2015)
What now beyond PVI for AF?
Can we target drivers more precisely?
Panoramic Mapping & AF ablation

- Potential to target mechanisms sustaining AF directly
- Potentially greater efficacy & less collateral damage
- Relatively new → outcome data limited
- Different systems available
  - CartoFlnder & CardioInsight systems at Barts
- Potentially different applications
- Could consecutive mapping catch up?
“Raw” AF Activation mapping – CARTOFINDER mapping system

• ‘Global mapping’ with basket catheters
• Simultaneous unipolar recordings 30s
CARTOFINDER MAPPING SYSTEM

• ‘Bipolar EGM window’ created
• Paired to 2 nearest poles
• Window covers bipolar EGMs
• Unipole annotated within window
• Peak negative $dv/dt$
Basket positioned in LA to achieve optimal coverage

Validation in Pacing
- Validation in Pacing
  - proximal & distal CS, roof and LAA (600ms)
  - ≥2 recordings was taken per patient
  - 2 blinded observers:
    - identify pacing site
    - ?earliest activation nearest pacing site

Validation in AT
- Validation in AT
  - Conventional LAT
  - Entrainment
  - Response to ablation
Cohort size 22 patients

1 patient excluded
Poor coverage & scarred LA

CARTOFINDER map analysis 56 ± 6s

LAT maps took 9.6 ± 7.4 min

Procedural duration 212 ± 57 min

Fluoroscopy time 4.0 min (IQR 3.1)

LA coverage 68.0 ± 10.2%
LA contact 74.2 ± 13.2%

172 CARTOFINDER maps
(8.2 ± 2.2 maps per patient)

21 patients included

84 maps during atrial pacing
88 during AT

27 ATs mapped
(1.4 ± 0.7 per patient)

CARTOFINDER map analysis 56 ± 6s

18 macro-reentrant ATs
9 focal/micro-reentrant ATs

21 patients included

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RESULTS: Validation with Pacing

• Pacing site identified in all cases

• Manual analysis confirmed that poles closest to pacing site were sites of earliest activation
  – Earliest activation recorded on up to four electrodes (2.3 ± 1.1)
  – Site of earliest activation on map was 1.8 - 8.2cm²
  – LAA vs. roof 6.7 ± 1.3cm² vs. 3.0 ± 0.8cm²; p<0.001
LA appendage pacing

S Honarbakhsh et al. J Cardiovasc Electrophysiol. 2017
## RESULTS:
### Validation in AT

<table>
<thead>
<tr>
<th>AT n</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>ATs mapped and ablated</td>
<td>27</td>
</tr>
<tr>
<td><strong>Mitral isthmus-dependent flutter</strong></td>
<td>6</td>
</tr>
<tr>
<td><strong>Roof-dependent flutter</strong></td>
<td>7</td>
</tr>
<tr>
<td><strong>Cavo-tricuspid isthmus-dependent flutter</strong></td>
<td>5</td>
</tr>
<tr>
<td><strong>Focal/micro re-entrant</strong></td>
<td>9</td>
</tr>
<tr>
<td><strong>LA mid anterior</strong></td>
<td>2</td>
</tr>
<tr>
<td><strong>LA mid roof</strong></td>
<td>3</td>
</tr>
<tr>
<td><strong>LA low antero-septal</strong></td>
<td>1</td>
</tr>
<tr>
<td><strong>LA low posterior</strong></td>
<td>1</td>
</tr>
<tr>
<td><strong>Right focal/micro-reentrant around scar</strong></td>
<td>2</td>
</tr>
</tbody>
</table>
Focal AT mapped to LA septum

S Honarbakhsh et al. J Cardiovasc Electrophysiol. 2017
Roof dependent flutter
CartoFinder Validation Conclusions

CARTOFINDER validated by mapping atrial paced beats & AT

Potential advantages:

1. Rapid mapping
2. Does not require sustained tachycardia or stable CL
Practicalities of basket mapping

- LA coverage with FIRMap > Constellation
  
  \(76.9 \pm 12.9\% \text{ vs. } 50.8 \pm 10.3\%; \ p<0.001\)

- Positioning catheter tip at or posterior to LA appendage ridge gave better coverage than a more lateral position

- Coverage inversely proportional to LA size

- Electrodes recording EGMs proportional to LA voltage

Honarbakhsh et al. JCE 2017
LA area & coverage

LA coverage, %

LA area (cm$^2$)

- Constellation catheter (R²=0.84, R=0.90, p<0.001)
- FIRMap catheter (R²=0.89, R=0.97, p<0.001)

Honarbakhsh et al. Heart Rhythm 2018
CartoFinder: insight into AF mechanisms

(1) Identify potential drivers using AF activation pattern

(2) Confirm relevance to AF maintenance by ablation response
Method: driver definitions

Potential driver, activation pattern:

• Focal, radial activation ≥2 consecutive wavefronts
• Rotational activity ≥1.5 rotations of 360 degrees

Confirmed driver, response to ablation:

• CL slowing ≥30ms
• Termination (SR/AT)
Method: confirmed driver characteristics

Offline analysis:

• Reproducibility

Proportion of CARTOFINDER maps showing the same driver

• Recurrence

Number of times driver identified during 30s recording

• Temporal stability

Number consecutive repetitions during each occurrence of driver
Method

- Persistent AF (<24 months)
- Baseline PentaRay CARTO bipolar voltage map
- CARTOFINDER basket maps pre & post-PVI (≥2 LA recordings)
- Post PVI, potential drivers identified on CARTOFINDER, ablated
  & ablation response used to confirm driver
29 pts.
154 maps (5.3 ± 1.3 /pt.)

Pre-PVI
22 potential drivers in 19 pts
1.4 ± 0.4 /pt.

Post-PVI
44 potential drivers in 29 pts
1.6 ± 0.8 /pt.

All 22 potential drivers identified pre-PVI also present post-PVI

39 confirmed drivers in all 29 pts.
1.3 ± 0.6 /pt.

Ablation response: 10 terminated to SR, 10 terminated to AT, 19 slowing CL
Confirmed driver with rotational activity on anterior wall
Results: confirmed driver characteristics

<table>
<thead>
<tr>
<th></th>
<th>Confirmed drivers</th>
<th>Focal</th>
<th>Rotational</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reproducibility, %</td>
<td>78 ± 19</td>
<td>83.4 ± 20.7</td>
<td>71.6 ± 17.5</td>
<td>0.03</td>
</tr>
<tr>
<td>% of maps driver seen in</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrence, mean ± SD N occurrences</td>
<td>8.7 ± 5.4</td>
<td>11.9 ± 6.2</td>
<td>6.3 ± 3.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Temporal stability, mean ± SD N repetitions</td>
<td>3.1 ± 0.9</td>
<td>3.4 ± 0.9</td>
<td>2.9 ± 0.8</td>
<td>0.07</td>
</tr>
<tr>
<td>AF termination n (%)</td>
<td>20 (51)</td>
<td>8 (50)</td>
<td>12 (52)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

S Honarbakhsh et al. Heart Rhythm 2018
Consecutive repetitions of a confirmed driver during each occurrence

- Focal with radial activation (over ≥2 consecutive wavefronts)
- Rotational activity (≥1.5 rotations of 360 degrees)
Conclusions

• Focal and rotational mechanisms identified in AF

• Drivers spatially conserved with temporal periodicity

• High rates of response to ablation

Termination of AF 69% pts (45% drivers)

Termination or CL slowing >30 ms all pts (89% of drivers)
Could EGM characteristics be used to identify drivers?

- EGM analysis in time and frequency domain
- Correlation hindered by difficulty identifying drivers
- We correlated EGM characteristics & drivers in 29 pts
- 29 pts mapped with Basket and Cartofinder EGM analysis
- Drivers correlated to markers rapidity & organisation
### Confirmed drivers & EGM characteristics

<table>
<thead>
<tr>
<th></th>
<th>Confirmed driver sites</th>
<th>Pts with ≥1 confirmed driver</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>co-locating</td>
<td>co-locating</td>
</tr>
<tr>
<td>(out of 39 drivers)</td>
<td>(out of 29 patients)</td>
<td></td>
</tr>
<tr>
<td><strong>Markers of Rapidity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fastest CL (shortest decile), n (%)</td>
<td>17 (44)</td>
<td>13 (45)</td>
</tr>
<tr>
<td>Highest DF (top decile), n (%)</td>
<td>15 (38)</td>
<td>11 (38)</td>
</tr>
<tr>
<td><strong>Markers of Organisation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lowest CLV (lowest decile), n (%)</td>
<td>29 (74)</td>
<td>25 (86)</td>
</tr>
<tr>
<td>Highest RI (top decile), n (%)</td>
<td>26 (67)</td>
<td>21 (72)</td>
</tr>
<tr>
<td><strong>CFAEs</strong></td>
<td>14 (36)</td>
<td>13 (45)</td>
</tr>
</tbody>
</table>
Focal driver on roof co-locating to site of lowest CL variability & highest DF

Honarbakhsh et al. Heart Rhythm 2018
Driver characteristics associated with AF termination

• Drivers with ↑ temporal stability
  (3.4 ± 0.9 vs. 2.7 ± 0.6 consecutive repetitions; p<0.001)

• Drivers identified on both pre & post-PVI maps
  (13/18, 72.2% vs. 3/14, 21.4%; p=0.001)

• Drivers co-locating to sites of EGM organisation
  lowest CL variability (20/29 vs. 0/10; p<0.001)
  highest RI (19/26 vs. 1/13 p<0.001)
Confirmed drivers & bipolar voltage

• Rotational drivers → LVZs
  
  (17/23, 74% rotational vs. 9/16 focal, 56% LVZs; p=0.31)

• ↑ LVZs predicted presence of rotational drivers
  
  (AUC 0.93, 95% CI 0.82-1.00; p=0.001)

• 49% of LA being LVZs predicted rotational driver
  
  (sensitivity 92.9%, specificity 77.8%)

→ Scar had no relationship to focal drivers
Can Drivers be identified on consecutive mapping?

- Markers of organisation promising correlation with drivers
- Can drivers be located through activation mapping through consecutive mapping?
- Region of Interest (ROI) algorithm on Cartofinder
- Focal and rotational detection algorithms
Definition of focal and rotational ROI

- **Focal:** 2 or more consecutive activations
  - S wave morphology
  - Focal activation pattern

- **Rotational ROI:**
  - Pan-systolic activation “wave”
  - EGMs in consecutive electrodes occupying >50% of local CL
  - distance <20mm containing CL
  - ≥2 cycles with 80% of Electrodes in compatible sequence
Rotational activation mapped with a Pentaray
Focal ROI mapped with basket and Pentaray

Honarbakhsh et al. JCE 2018
Consistency identifying focal ROI with Pentaray

- 86% of focal activations identified as ROI
- 23 patients mapped with both basket and PentaRay
- 22/30 (73%) focal drivers identified as ROI with PentaRay
- ROI identified on Pentaray:
  - greater temporal stability (3.6±0.6 vs. 2.7±0.6; p<0.001),
  - higher recurrence rate (12.4±2.7 vs. 7.2±0.9; p<0.001),
  - more frequently associated with AF termination (p<0.001)

Honarbakhsh et al. JCE 2018
Optimizing sequential mapping: OctaRay mapping

Perseid 2-2-2.
D-1609-01-SI

Galaxy 2-5-2.
D-1609-02-SI

Galaxy 3-3-3.
D-1609-03-SI

30 mm span

40 mm span
Conclusion on CartoFinder

• Focal and rotational activations observed
• Spatially conserved but temporal periodicity
• Acute response to CartoFinder ablation promising
• Ablation guided by basket best tested
• Consecutive mapping similarly effective identifying drivers
• Markers of organisation and ROI very sensitive & specific
Panoramic mapping with the ECGI
Determine Heart-Electrode Anatomy

Patient lies in supine position

CT scan
Segmentation algorithms
Manually edit geometry

Vest included in scan field of view

Electrode labeling algorithms
Producing maps from surface EGMs

Record data → Phase mapping → Display drivers

Inverse problem → Inverse problem → Feature Extraction → Feature Extraction
Phase mapping

AF WORKFLOW

Define phase intervals
Identify intervals with >1000ms (recommend 1200ms) over enough samples (ex. 10+) to be representative of rhythm under investigation.

Create phase maps
Create a playable phase map for each processed map interval

Phase map analysis
Analyze each phase map to verify rotation and focal detections

Composite map
Displays composite of all detected phase map activity

Interval1

Segment CT and combine AF recordings
Examples of a Drivers (Rotors and Focal)
Phase Map displays activation patterns as they progress through the heart.

Composite Map
1. Focal detections (white dots)
2. Rotational area (orange areas)
Driver Domains in Persistent Atrial Fibrillation

Methods
• Driver ablation guided by ECGI
• Ablation strategy: driver ablation (clusters) ± PVI (if drivers adjacent to/in PVs), then PVI and linear lesions if AF not terminated.

Results
AF termination 82/103 patients (80%)

Average RF duration to terminate AF
ECGI group: 28 +/- 17 min.
Matched controls: 65 +/- 33 min.

Outcomes:
90/103 reached 12 month follow-up
58/90 (64%) SR at 12 months
16/90 repeat ablations for atrial tachycardia (12) or AF (4)
85% SR with AF termination
AFACART Trial

- Multicenter (8 centers) without prior ECG-I experience
- 118 patients, non-randomized
- N=118, PsAF <1 year, refractory to >1 AAD, LA <55mm
- Primary endpoint: termination of AF

Diagram:
- Driver Ablation → PVI → Lines → No AF Term
- PVI → Lines → AT → DCC
- NSR → AT → DCC
AFACART Trial

4.9 + 1.0 drivers
81% re-entrant
19% focal
AFACART Trial

• Driver ablation terminated AF in 75 of 118 patients (64%)
• 2 additional patients terminated with PV isolation
• 8 terminated with lines (Step 3)
• AF termination in 72%.
• Driver ablation alone caused termination or AFCL prolongation >10% in 94% of patients

• Termination with RF duration of 46+/-28 min
• Overall RF duration 75+27 min
AFACART Trial

**Top Diagram:**
- No acute termination: 100%
- Acute termination: 0%
- *P* = 0.672 for comparison across all centres

**Bottom Diagram:**
- AF recurrence: 100%
- No AF recurrence: 0%
- *P* = 0.048 for comparison across all centres
AFACART Trial

76% free from AF
39% free from AF and AT
AFACART Trial

- Termination of AF promising
- High rates of AT in this protocol (38%)

- 65% of AT recurrences macro-re-entrant
- 49% of macro-re-entrant ATs related to gaps in lines
- Of the 35% of non-macro-re-entrant Ats, 75% were located at sites of drivers during index procedure

- Interesting proof of concept study
- Is it the best work flow for clinical outcome?
Conclusions

• Insight into mechanisms of AF
• Early data now for AF and AT
• AFACART proof of concept
  → Locate drivers in persistent AF
  → Targeting drivers interrupts AF mechanisms
• Easy add on to work flow
• Several potential uses in AF ablation
Identification of drivers outside PVs

Median rotations 2.6 (IQR 2.3–3.3)
Identification of drivers outside PVs

* = Faci in % patient
** = Rotor in % patient

Haissaguerre M et al., Circulation. 2014
Duration of AF and number of drivers

Driver regions

- Persistent in SR
- Persistent (1-3m)
- Persistent (4-6m)
- Persistent (7-9m)
- Persistent (10-12m)
- Long-Lasting
Duration of AF and distribution of drivers

- **PersSR**
  - Extra-PV: 31%
  - PV: 69%

- **Pers<12m**
  - Extra-PV: 55%
  - PV: 45%

- **Pers>12m**
  - Extra-PV: 75%
  - PV: 25%
Potential for ECGI at each stage

- **DIAGNOSIS & STRATIFICATION**
  - Optimal treatment path

- **PRE-TREATMENT PLANNING**
  - Optimal treatment planning

- **DYNAMIC MAPPING DURING ABLATION**
  - Dynamic feedback
ECG-I targeted ablation for persistent AF (ECG-I TARGET AF).

50 patients with persistent AF

↓

PVI

ECG-I guided targeting of drivers to terminate AF

↓

1 year follow up
ECG-I phenotyping of persistent AF based on driver distribution to predict response to PVI (ECG-I PHENOTYPE AF).

100 pts with persistent AF

ECG-I mapping to determine driver distribution

PVI using cryoballoon

1 year follow up
ECG-I targeted ablation for persistent AF not responding to PVI: results of a 2 staged strategy (ECG-I TARGET AF 2).

Patients with recurrent AF following Cryo for persistent AF (Those with recurrent AF from ECG-I PHENOTYPE AF)

Estimated enrolment 50 patients

↓

Repeat PVI

ECG-I guided targeting of drivers to terminate AF

↓

1 year follow up
Phenotype AF progress

• 77/100 patients enrolled
• HRC poster on first 36 patients
• ECGI recordings pre and post Cryo PVI
• Potential Drivers (PDs) defined:
  Rotational activation completing ≥ 1.5 revolutions
  Focal activations
Phenotype AF: Early acute results

6/36 PVI terminated to SR
42 ± 17 PD occurrences per patient
Pre PVI: 12 ± 3 segments (of 18) harbouring drivers

Post PVI
20% ↓ segments harbouring PDs outside PVs & Post Wall
    (9.1 ± 2.2 vs 7.2 ± 3.5, p = 0.002)
15% ↓ driver occurrences outside PVs & Post Wall
    (35 ± 13.9 vs 29.6 ± 13.8, p = 0.029)

Termination of AF
Total no. PDs pre PVI predicted AF Termination (p = 0.044)
Total no. segments trended to significance (p = 0.053)
ROC Curve demonstrating factors predicting termination of AF

Total no of PDs: AUC 0.764, 95% CI 0.555 - 0.973, p = 0.044. 30 PD cut off = Sensitivity of 66.7% and Specificity of 80%.

Total no of segments: AUC 0.753, 95% CI 0.578 – 0.927, p = 0.053) ≤ 12 segments cut off = sensitivity of 83.3% and specificity of 60%.
Conclusions panoramic mapping

• Fascinating insights into AF mechanisms
• Focal & rotational activations
• Spatially conserved but temporal periodicity
• Good acute results – outcome data needed
• Activation mapping in AF has advantages
• May be able to replicate with consecutive mapping
• ECGI may have uses outside cath lab