

## Substrate mapping of the left atrium in persistent atrial fibrillation: spatial correlation of localized complex conduction patterns in global charge-density maps to low-voltage areas in 3D contact bipolar voltage maps

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### Objective

Characterization of low-voltage areas (LVAs) as a surrogate of left atrial substrate with bipolar voltage mapping (BVM) is increasingly being used for the treatment of PsAF. Application of a global, non-contact, charge-density based imaging, and mapping system (AcQMap, Acutus Medical, Carlsbad CA) (AcM) in PsAF has led to the identification of distinct localized complex conduction (LCC) patterns that may be relevant in the initiation and maintenance of PsAF. This study aimed to investigate the spatial relationship between of LVAs in bipolar BVM and LCC-cores identified with the AcQMap system.

### Key Points

- Wave front direction-dependent discrepancies observed in the spatial distribution of LVAs identified from BVM.
- LCC-cores mapped during PsAF only partially co-localize with LVAs and are predominantly localized at border zones of the LVA, also known as heterogenous scar.
- These findings limit the usage of BVM in the identification of atrial substrate for determining a patient tailored ablation strategy for the treatment of PsAF.

### Methods

- 10 patients with PsAF, first redo post index cryo ablation with confirmed PVI.
- High density BVM made with CARTO and PentRay in SR, pacing at 600msec from CSd and CSp.
- 10sec of AcQMap AF maps to identify LCC cores with automated LCC (LIA, LRA and Focal) detection software 'AcQTrack.'

- Customized analysis tool used to assess.
  - Spatial overlap between BVM with varying wave-fronts directionality with LVA cutoff of 0.2 and 0.5mV.
  - Creation of BVM composite maps with composite cutoff 0.2 to 1mV.
  - Spatial overlap between composite maps and LCC-cores.
  - Minimal distance from LCC-cores to the border of composite LVA.
- Point-by-Point (PBP) datafiles (3650 points per patient) of LCCs counts and Bipolar Voltage Amplitudes (BVA) were generated to assess.
  - Correlation of BVA between SR, pacing CSd and pacing CSp.
  - Sensitivity/specificity and AURC calculations for composite BVA and LCC counts.
  - Cohen's Kappa coefficient to determine inter-rater reliability between composite BVA and LCC counts.

### Results

- The average bipolar amplitude is significantly different when varying wave-front directionality.
- The percentage spatial overlap of the LVA between SR, pacing CSd and CSp are comparable between groups, ranging from 21.09 to 37.7%. Correlation coefficient based on PBP comparative analysis was low, ranging from 0.31 to 0.43.
- The percentage spatial overlap between LVAs and LCC-core patterns detected by AcQTrack increased with increasing LVA cut-off values. LIA had a significantly higher overlap with LVA compared to LRA and Focal patterns when LVAs were defined by voltages equal to or higher than 0.5 mV.

- The average distance from the LCC-core to the border of the LVA was  $28.41 \pm 15.56$  mm,  $29.03 \pm 19.57$  mm, and  $35.62 \pm 19.78$  mm for LIA, LRA and Focal LCC patterns, respectively.
- LVA showed low sensitivity and high specificity for LIA, LRA, and Focal patterns. AURC was 0.46, 0.48, and 0.39 for LIA, LRA and Focal respectively.
- Cohen’s kappa coefficient was  $-0.06 \pm 0.01$ ,  $-0.08 \pm 0.01$ , and  $-0.08 \pm 0.01$  for LIA, LRA, and Focal patterns, respectively.

LVA Definition mV	Spatial Overlap %	Spatial Overlap %	Spatial Overlap %	p values	p values	p values
	LIA with LVA	LRA with LVA	Focal with LVA	LIA vs LRA	LIA vs F	LRA v F
0.2	4.97 ± 7.39	3.27 ± 5.25	1.09 ± 1.92	0.173	0.101	0.139
0.3	7.21 ± 9.02	4.52 ± 6.54	1.91 ± 2.70	0.092	0.075	0.161
0.4	9.60 ± 10.51	6.06 ± 7.76	3.12 ± 3.72	0.054	0.060	0.175
0.5	12.59 ± 11.81	7.80 ± 9.20	4.62 ± 5.27	0.020	0.036	0.187
0.6	16.40 ± 12.92	10.30 ± 10.37	6.02 ± 5.98	0.009	0.012	0.103
0.7	19.87 ± 14.41	11.83 ± 11.47	7.34 ± 6.93	0.003	0.005	0.103
0.8	23.4 ± 15.75	13.53 ± 11.52	7.85 ± 7.05	0.003	0.002	0.056
0.9	26.94 ± 16.95	15.28 ± 11.37	9.76 ± 8.80	0.003	0.002	0.107
1	30.30 ± 18.67	17.01 ± 11.65	9.32 ± 6.98	0.004	0.001	0.023

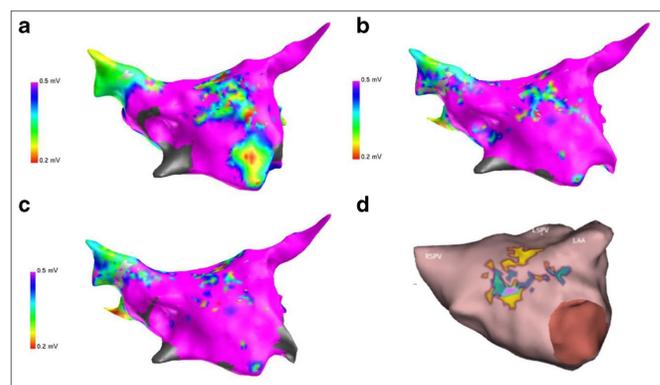
**Table 1:** Spatial Overlap of LIA/LRA/Focal patterns determined by AcQTrack and with LVA determined by composite maps.

### Study Limitations

- Small patient population, partially mitigate by large point by point comparison.
- Heterogenous patient population in percentage of LVA.
- No CARTO BVM were made in AF.

### Conclusion & Clinical implication

- Wave front direction-dependent discrepancies observed in the LVAs identified from BVM imply that guidance of ablation strategies in the treatment of patient with PsAF is questionable with this method of substrate characterization.
- The largest discrepancies appear to lie within the most heterogeneous substrate, which are also more likely to be involved in initiating and maintaining PsAF.
- LCC pattern-cores observed during PsAF are only partially colocalized with LVAs identified with BVM.
- This significantly limits the usage of LVAs acquired from a single, unidirectional wave front as a surrogate for substrate mapping to identify clinically relevant LCC-cores in PsAF.



**Fig. 1:** LA Anatomy in AP view. a, b, and c represent bipolar voltage maps made in sinus rhythm, pacing coronary sinus distal and coronary sinus proximal at 600 ms respectively. d represents AcQTrack data where yellow, green and purple means high concurrencies of LIA, LRA, and Focal patterns respectively. LIA localized irregular activity; LRA localized rotational activation.

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#### ABOUT ACUTUS MEDICAL

Acutus Medical is a dynamic arrhythmia care company focused on developing distinct, innovative technologies designed to provide physicians and patients with improved results. Founded in 2011, Acutus Medical, Inc., is based in Carlsbad, California.



#### U.S. Indication for Use:

The AcQMap System is intended for use in patients for whom electrophysiology procedures have been prescribed.

When used with the AcQMap Catheters, the AcQMap System is intended to be used to reconstruct the selected chamber from ultrasound data for purposes of visualizing the chamber anatomy and displaying electrical impulses as either charge density-based or voltage-based maps of complex arrhythmias that may be difficult to identify using conventional mapping systems alone.

AND – When used with the specified Patient Electrodes, the AcQMap System is intended to display the position of AcQMap Catheters and conventional electrophysiology (EP) catheters in the heart.

OR – When used with conventional electrophysiology catheters, the AcQMap System provides information about the electrical activity of the heart and about catheter location during the procedure.

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