Subject-Specific Ablation of Pathologic Conduction Patterns Beyond the Pulmonary Veins: A Personalised Modelling Approach

Ovais A.Jaffery[1], Caterina Vidal Horrach[1], Daniel J.Lagalante[3], George Thomas[2], Gregory Slabaugh[1], Lea Melki[3], Wilson W.Good [3], Caroline H.Roney [1]

[1] Queen Mary University of London, UK [2] Weill Cornell Medicine, New York, USA
[3] Acutus Medical, Carlsbad CA, USA

Abstract

Improving patient outcomes with ablation of non-paroxysmal AF (PsAF) has proved challenging using a population-based treatment approach due to large interindividual variability in the underlying electroanatomical substrate. Ablation of pathologic conduction patterns outside of pulmonary vein isolation (PVI) has recently shown encouraging results in PsAF patients returning for their first or second retreatment (76% freedom from AF recorded in the RECOVER AF trial). However, the optimal targets and best sequence of ablation lesions are still unknown, and testing different sequences, types, and methods of ablation cannot be performed clinically on a single patient or patient cohort. Considering the predictive potential of computational modelling, a small exploratory subset of patients (N=4) enrolled in the ongoing DISCOVER trial was used to create patient-specific models of left atrial electrophysiology. The subject-specific models displayed a high correlation between simulated targets and clinical targets. AF complexity was highest in all patients prior to therapy. PVI caused a marginal decrease in complexity across the cohort whereas PVI+PCP showed an extensive decrease in the AF complexity across the patients and resulted in AF termination in all patients.

1. Introduction

Atrial fibrillation (AF) is an abnormal rhythm that affects more than 43 million people worldwide [1]. Long-term success with ablation therapy in patients with persistent AF remains elusive with outcomes between 38% and 64% at 12 months, often necessitating second, third, and even fourth procedures to achieve sustained sinus rhythm (SR) [2]. Despite high patient-to-patient variability, the gold standard treatment of AF and even atrial flutter is still generalized to pulmonary vein isolation (PVI) which provides moderate performance in achieving long-term freedom of AF [3], particularly in patients with persistent AF.

As such, novel ablation approaches targeting areas outside of the pulmonary veins (PV) are required. Targeting subject-specific, non-PV pathologic conduction patterns (PCP) - including focal, local irregular activity (LIA) and local partial irregular rotation (LPRA) - observed during AF has recently shown encouraging results in persistent AF patients returning for their first or second retreatment (76% freedom from AF) [2]. However, the effects of ablation of each area of pathologic conduction, and the most effective ablation approach is unknown, and difficult to test clinically.

Personalised computational models calibrated to a patient's conduction properties can be used to investigate the effects of different ablation approaches, to investigate the effects on AF mechanisms, and to optimise ablation approaches. This study aims to assess the efficacy of sequential PCP ablation strategies using subject-specific computational modeling with the goal of maximising predictive accuracy while minimising the amount of tissue ablated per patient.

2. Patient Personalisation Pipeline

Subject-specific models were created for a small exploratory subset of patients (N=4) enrolled in the ongoing DISCOVER trial [4], which is an observational, prospective, multi-center, open-label registry of procedural and long-term clinical outcomes. Generation of a left atrial model personalized to patient electroanatomic mapping (EAM) data entails the following steps.

2.1. Data Acquisition

Anatomical models and associated conduction velocity (CV) were obtained using the AcQMap system (Acutus Medical, Carlsbad). Pathologic conduction regions detected by the AcQTrack system [5] in the form of focal, LIA and LPRA were exported for offline analysis, alongside geometry and CV data. In addition, composite maps

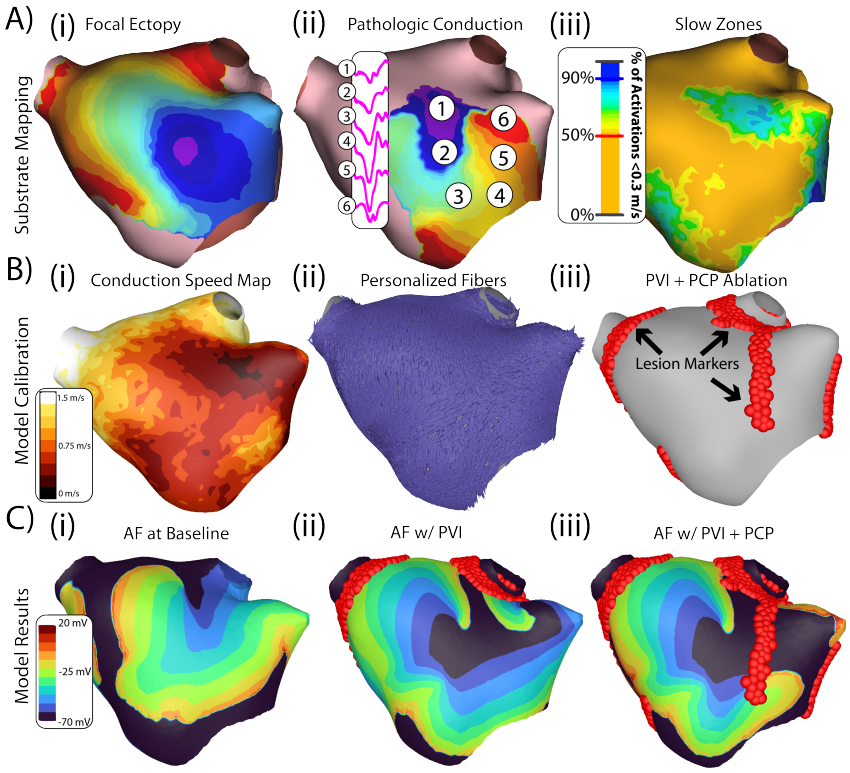

Figure 1. In-silico Ablation Pipeline for PVI and PVI+PCP Ablations using AcQMap CV Data.

were generated with a threshold of 0.3 m/s CV, and slow zones detected in the composite maps were also exported. Fig. 1A(i-iii) shows an example of pathologic conduction detection, along with a composite map generated to detect slow zones.

2.2. Personalized Anatomical Geometry

The starting point for the creation of a patient-specific geometry is the anatomical data generated during an EAM procedure in the form of a shell geometry, which is a surface representation in 3D space. First, the 3D shell obtained from the EAM system was preprocessed by clipping PVs in Paraview software, and remeshed to a resolution of 300 microns using meshtools. Landmark points were selected on the geometry using an in-house python code to seed the points needed for the identification of PVs, appendage and MV. Next, universal atrial coordinates [6] were calculated for each patient-specific shell geometry, and atlas-based fibers were assigned to the geometry, using methods described by Roney et al. [7].

2.3. Calibration, Simulation and Target Identification

Monodomain model tissue conductivity parameters were calibrated to clinical CV data by assigning zones of conductivity to different ranges of CV (Fig. 1B(i)) using a pre-computed conductivity - CV mapping. Simulations of parameterized subject-specific models were performed using the CARP simulation framework [8], with the Courtemanche et al. human atrial cell model. Initial conditions to initiate AF were applied corresponding to four spiral wave re-entries, and AF was simulated for 5000 ms. Fig. 1C(i) shows an example simulation of AF on a model calibrated to patient CV data. To post-process AF data, characterize conduction patterns, and identify potential ablation targets, phase singularity (PS) density maps were calculated using simulated membrane potentials following our previous study [9]. Regions of high AF complexity were identified using hot spots on PS density maps.

Simulated ablation targets were identified through a combination of clinical and simulation inputs including AcQTrack system PCP-targets, slow zones observed in AcQMap composite maps, simulated hot spots computed in PS maps, and the simulated AF propagation wave patterns for the calibrated LA models. Examples of in-silico targets and ablation lesions are shown in Fig. 1C(iii).

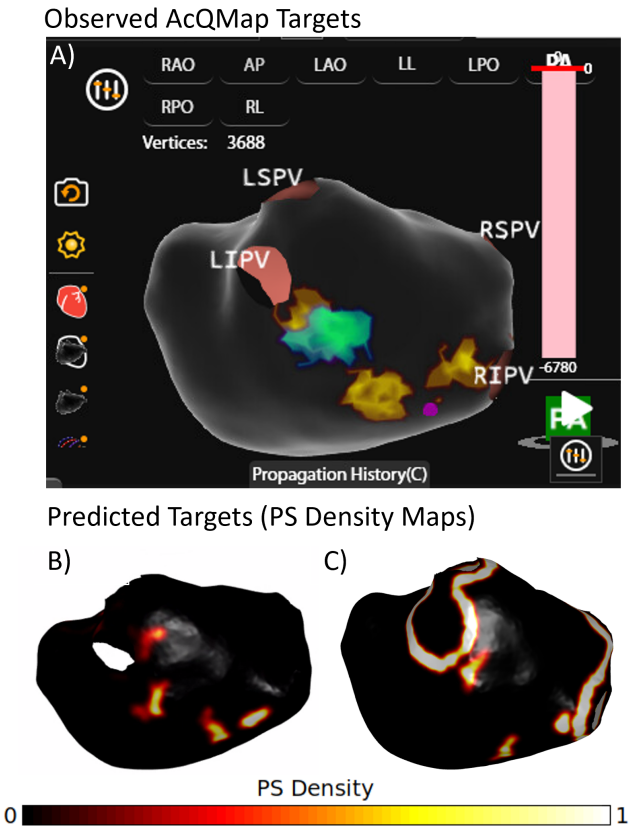

Figure 2. Comparison of Acutus AcQTrack PCP targets and PS targets computed using the calibrated LA model, demonstrating a good visual agreement. A) LIA, LPRA and focal targets are indicated by green, mustard and pink colors respectively. B) PS Density Map of simulated AF. C) PS Density Map after application of PVI ablation.

2.4. Pathologic Substrate Based Ablations

The ablation lesion regions were assigned conductivity values close to 0 (0.001) during the simulation step to make the ablated tissue inert to activation. A stepwise ablation strategy based on AF complexity of the identified targets and wave propagation patterns was developed. All patient cases were first simulated with PVI ablation, followed by stepwise PCP ablation. Non-conducting cores for a given ablation target were selected based on wave propagation direction with the aim of containing wave propagation. This strategy to ablate and connect identified targets to inert boundaries was simulated as shown in Fig. 1C(ii-iii).

3. Results and Discussion

A good agreement was observed between the personalized model and AcQMap targets; an example is shown in Fig. 2(A-C). PS density maps were compared pre and post PVI ablation; comparison shown in Fig. 2(B) and (C). Remapped targets identified through PS density map after PVI ablations were used to identify PCP ablation targets.

A representative simulated ablation case is shown in Fig. 3 where the step wise decrease in AF complexity is depicted after each in-silico ablation lesion is added to the simulation (Fig.3A-C). Complete termination of AF is only achieved after multiple PCP ablations are performed. For all cases, additional ablations either in form of a PV-MV line or roof line or both were required to revert the model from flutter to sinus rhythm (SR), as shown in Fig. 3D(i-ii).

A comparison of the contribution of the two ablation types (PVI and PCP) towards changes in AF cycle length (AFCL) and ablated tissue area per patient is shown in Table 1. The reduction in AF complexity is quantified by an increase in AF cycle length (shown as ΔAFCL) for the cohort of patients considered in the study.

Case	AFCL (ms)	ΔAFCL (ms)		LA (cm^2)	Ablated (cm^2)	
		PVI	PCP		PVI	PCP
1	180	24	56	163	11.87	6.91
2	144	60	107	171	13.05	4.57
3	158	38	61	144	12.05	5.08
4	177	27	48	152	13.95	6.52

Table 1. PVI and PCP Ablation Comparison

In all four cases, both PVI and PCP ablations contribute towards CL increase. PCP ablation caused a larger increase in AFCL, compared to PVI alone. The corresponding tissue areas ablated with PCP ablation is comparatively less in all cases. Wavefront propagation comparison between simulated pre-ablation, post-PVI and post-PVI+PCP ablations show that in all cases PCP ablation was required to eliminate fibrillatory patterns. These results demonstrate the importance of PCP ablation, and motivate an innovative study into the effect of PCP ablation across a larger clinical population to validate these initial results.

4. Conclusion

This study used a stepwise ablation approach in subject-specific computational models to provide a means to guide effective therapy toward optimal patient outcomes. Targeting pathologic propagation identified during AF effectively reduces AF complexity, and potentially improves long-term freedom from AF.

Acknowledgments

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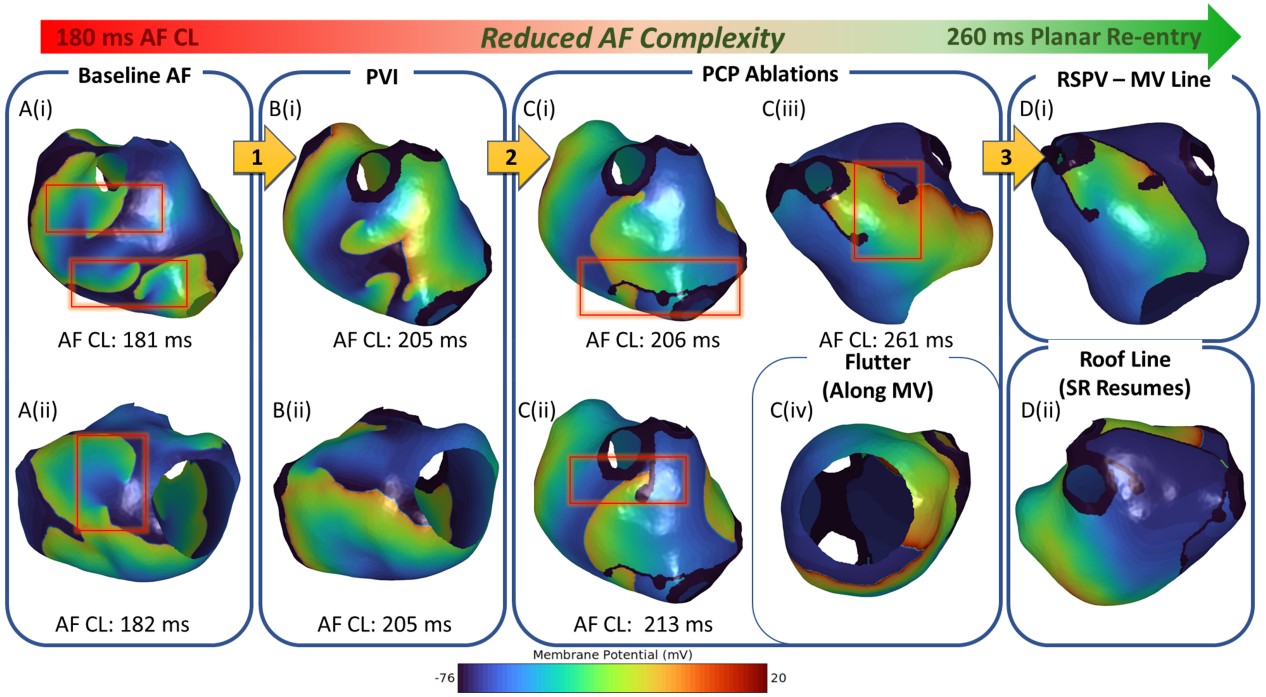

Figure 3. In-silico PCP ablation decreases AF complexity in a patient-specific LA model. Sequential ablations following PVI are shown, together with AFCL calculated at regions of high AF complexity (depicted by red colored boxes). PCP ablations decrease AFCL, and lead to AF termination to flutter. A final roof line leads to sinus rhythm (SR).

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Address for correspondence:

Ovais A. Jaffery

Queen Mary University of London, UK (o.jaffery@qmul.ac.uk)