Modeling Myocardial Fibrosis Improves ECG-Based Inference in Dilated Cardiomyopathy

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Abstract

Myocardial fibrosis is a key structural feature of dilated cardiomyopathy (DCM) and alters ventricular activation, however reduced-order models used for ECG fitting usually model it into a globally reduced conduction velocity. We investigated whether representing fibrosis explicitly improves the approximation of the QRS complex in two patients with idiopathic DCM. Patient-specific fibrotic regions were segmented by a clinician from late gadolinium-enhanced magnetic resonance imaging (LGE-MRI) and included to a reduced-order Eikonal model as a distinct, slowly conducting region whose velocity was inferred alongside the tissue velocities and earliest-activation sites. We compared four personalisation scenarios: a reference solution without fibrosis, explicit fibrosis modeling, and two variants in which the reference conduction velocity priors were globally scaled down to 80% and 60%. Explicit fibrosis improved the fit over the reference in both patients, raising the mean Pearson correlation coefficient (PCC) from 0.920 to 0.947 and from 0.885 to 0.895, respectively, and reducing the root mean square error (RMSE) in both. Global scaling down the CVs reached a higher PCC, but depended on the chosen factor: scaling to 60% degraded the fit in one patient below the reference. The inferred fibrotic velocity (0.11 and 0.18 m/s) was weakly constrained by the QRS. These findings suggest that explicitly modeling fibrosis provides a more physiologically consistent representation in DCM and improves ECG-based inference, supporting its inclusion in reduced-order cardiac digital twin models.

1. Introduction

Dilated cardiomyopathy (DCM) is frequently accompanied by myocardial fibrosis, which slows electrical propagation and is a substrate for conduction abnormalities. Characterising this substrate non-invasively from routinely acquired data is clinically relevant, but requires a model that links the underlying tissue properties to the measured electrocardiogram (ECG).

Cardiac digital twins constrained by clinical data are becoming a useful tool for this task. Reduced-order models, in which ventricular activation is described by an Eikonal model, make it tractable to infer the conduction velocities and earliest-activation sites from the 12-lead ECG by Bayesian inference [1, 2]. In such models, however, fibrosis is typically not represented explicitly; its effect is instead modeled into a globally reduced conduction velocity, even though the fibrotic substrate is spatially localised.

In this work, we extend a reduced-order Eikonal–SMC-ABC framework [1, 2] by adding LGE-derived fibrotic regions to the forward model as a distinct, slowly conducting region, whose conduction velocity is inferred alongside the tissue velocities and earliest-activation sites. In this work, we analyze whether this explicit representation improves the fit of the simulated QRS to the clinical ECG in DCM, compared with globally reduced velocities.

2. Methods

2.1. Clinical data

Two patients with idiopathic dilated cardiomyopathy (Patients 1 and 10) were selected at the University Hospital of the Federal University of Juiz de Fora. For each patient we extracted the 12-lead ECG, of which eight independent leads (I, II, V1–V6) and a late gadolinium-enhanced magnetic resonance image (LGE-MRI). The QRS complex of each lead was pre-processed using the same technique as described in Camps et al. [2].

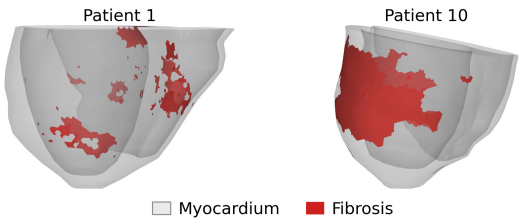

Figure 1: Biventricular meshes of Patients 1 and 10 with the segmented fibrotic regions. The myocardium is rendered translucent to expose intramural fibrosis.

2.2. Mesh generation pipeline

The MRI data was processed using the same methods described in Namorato et al. [3] and the segmented fibrosis mapped onto each mesh as a binary nodal mask. Patient-specific biventricular tetrahedral meshes and fiber orientation fields were generated with the open-source INSILICOHEARTGEN software [4] with a mean edge length of 1.5mm and compatible with the reduced-order Eikonal–SMC-ABC framework [2], as can be seen in Figure 1.

2.3. Personalisation method

In this work, we adapt the open-source reduced-order personalisation framework of Camps et al. [1, 2]. Ventricular activation was modelled with an Eikonal model solved on the tetrahedral mesh with a Dijkstra-like shortest-path algorithm, yielding a local activation time (LAT) at every node. A rule-based Purkinje network was generated from the ventricular coordinates, and activation was initiated at a set of endocardial root nodes. The QRS complex was then computed from the LAT map with a pseudo-ECG formulation using a step-function source model.

Anisotropic conduction was parameterised by five velocities, along the fibre, sheet and normal directions, and two endocardial velocities (a fast dense and a sparse layer). To model fibrosis explicitly, the cost of every mesh edge falling within the binary nodal fibrotic mask was set to its length divided by an additional fibrotic conduction velocity, so that propagation through fibrotic tissue was slowed. The fibrotic velocity was inferred jointly with the remaining parameters.

The inverse problem, recovering the conduction velocities and the number and location of the root nodes from the clinical QRS, was solved with a sequential Monte Carlo approximate Bayesian computation (SMC-ABC) scheme [1]. The method jointly infers continuous parameters (the conduction velocities) and discrete ones (the root nodes configuration). At each iteration the worst half of the population is discarded and replaced by perturbed copies of the retained particles through Markov chain Monte Carlo moves, accepted only if their discrepancy falls below an adaptive threshold. The discrepancy between a simulated and the clinical QRS combined the root mean square error (RMSE) of the eight leads with their Pearson correlation coefficient (PCC), weighted so that the morphological (PCC) term dominates the amplitude (RMSE) term. A physiological constraint enforcing a faster dense than sparse endocardial layer was imposed. The prior ranges and the main inference settings are listed in Table 1; they were kept identical across patients and across all modelling scenarios, except for the additional fibrotic velocity in the fibrosis case.

Table 1: Prior ranges for the inferred parameters and main inference settings. Conduction velocities are given in m/s.

Parameter	Prior range
Fibre velocity	0.4–0.8
Sheet velocity	0.3–0.6
Normal velocity	0.3–0.5
Dense endocardial velocity	1.0–1.9
Sparse endocardial velocity	0.4–1.5
Fibrosis velocity	0.1–0.2
Purkinje velocity (fixed)	3.0
Number of root nodes	3–9 (mean 6)
Population size	128
MCMC steps per iteration	100
Retain ratio	0.5

Conduction velocity ranges were based on Durrer et al. [5].

For each patient we ran the inference under four scenarios: 1) Reference personalisation; 2) Explicit fibrosis modelling; 3, 4) and two variants in which fibrosis is again absent but the reference CV priors are globally scaled down by 80% and 60%, respectively.The best result from the inference process, i.e. the one with the lowest discrepancy, was used for all reported results.

3. Results and discussion

Table 2 reports the QRS fit under four modelling assumptions. Representing fibrosis explicitly improved the agreement between simulated and clinical QRS in both patients relative to the reference: the mean PCC increased from 0.920 to 0.947 in Patient 1 and from 0.885 to 0.895 in Patient 10, with a concurrent reduction in RMSE in both cases.

Globally scaling the CV priors down to 80% also improved the fit over the reference, reaching an agreement comparable to the explicit fibrosis scenario (PCC 0.951 versus 0.947 in Patient 1, and 0.902 versus 0.895 in Patient 10). Neither approach dominated: the scaled priors gave the higher PCC in both patients, whereas explicit fibrosis gave the lower RMSE in both, so the two differ in how they distribute the residual between morphology and amplitude. The global reduction was, however, sensitive to the chosen factor. Scaling to 60% degraded the fit in Patient 10 below the reference (PCC 0.855), with the inferred

Table 2: QRS fit and inferred conduction velocities for Patients 1 and 10 under four modelling assumptions: the reference personalisation without fibrosis; explicit fibrosis; and two variants without fibrosis in which the conduction velocity (CV) prior bounds were globally scaled down to 80% and 60% of their reference values. PCC: Pearson correlation coefficient; RMSE: root mean square error. Velocities in m/s. Fibrotic burden (in brackets) is the volume-weighted fraction of ventricular tissue labelled as fibrotic. Best value per patient and metric in bold.

		QRS fit		Inferred conduction velocity (m/s)					
Patient	Scenario	PCC	RMSE	Fibre	Sheet	Normal	Endo_d	Endo_s	Fibr.
1 (14%)	Reference	0.920	0.265	0.53	0.32	0.41	1.08	0.87	–
	Global CV 80%	**0.951**	0.214	0.42	0.26	0.28	1.42	0.83	–
	Global CV 60%	0.946	0.239	0.32	0.20	0.24	0.66	0.66	–
	Explicit fibrosis	0.947	**0.213**	0.47	0.30	0.36	1.28	0.79	0.11
10 (15%)	Reference	0.885	0.259	0.42	0.37	0.42	1.13	1.05	–
	Global CV 80%	**0.902**	0.254	0.51	0.45	0.28	0.97	0.74	–
	Global CV 60%	0.855	0.272	0.48	0.26	0.21	0.88	0.70	–
	Explicit fibrosis	0.895	**0.248**	0.48	0.25	0.46	1.31	0.82	0.18

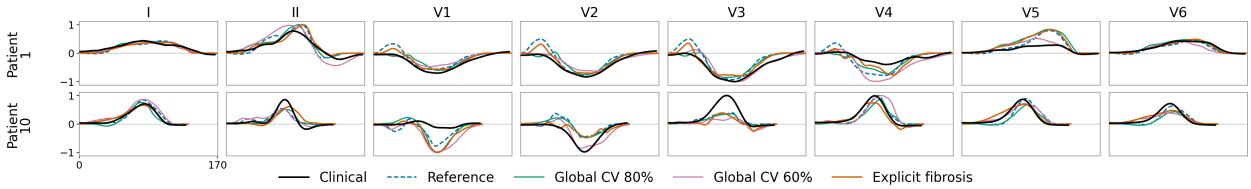

Figure 2: Clinical and simulated QRS for the eight leads in Patients 1 (top) and 10 (bottom), for the reference personalisation, the two globally scaled down conduction velocities and explicit fibrosis. Amplitudes are normalised within each patient.

fibre velocity pinned at the upper bound of the scaled prior, indicating that the data required faster conduction than the prior allowed. Explicit fibrosis improved the fit in both patients without such a factor having to be chosen.

In both patients the inferred fibrotic conduction velocity was slow (0.11 and 0.18 m/s), two- to four-fold slower than the inferred fibre velocity. These values, however, span essentially the whole prior (0.10–0.20 m/s) and lie close to its bounds, so the QRS does not strongly constrain this parameter: its posterior is largely prior-determined and the value should be read as an order of magnitude. This weak identifiability is consistent with the known difficulty of uniquely recovering conduction parameters from the surface ECG [6], and suggests that the benefit of modelling fibrosis lies in reshaping the activation spatially rather than in recovering a specific velocity.

The inference also recovers the number and endocardial location of the earliest activation sites: seven in Patient 1 and six in Patient 10, both within the prior range (3–9). Across the final population these locations were spatially structured rather than diffuse (Figure 3), with left-ventricular activation initiating from a single mid-septal site in Patient 1 (in 100% of the population) and from the basal anterior wall and apex in Patient 10. The recovered patterns are consistent with a predominantly septal-to-apical onset of activation, supporting the physiological plausibility of the personalisation. Figures 2 and 4 show, for both patients, the simulated versus clinical QRS and the local activation time maps. Introducing the fibrotic region locally slowed conduction and reshaped the activation wavefront around the segmented tissue, which translated into a closer match of the simulated QRS morphology to the clinical tracing. In Patient 10, the fibrotic region fell in a comparatively late-activating portion of the myocardium (median local activation time 71 ms, against 64 ms for the myocardium as a whole, in the no-fibrosis baseline), and its explicit representation still improved the fit, indicating that the benefit is not confined to fibrosis lying on the earliest activation pathways.

4. Conclusion

By extending the reduced-order Eikonal–SMC-ABC framework to represent myocardial fibrosis explicitly and to infer its conduction velocity jointly with the activation parameters, we obtained a closer fit to the clinical QRS in both patients with idiopathic DCM, compared with the reference personalisation, and without having to choose a global scaling factor. The inferred fibrotic conduction velocity was slow (0.11 and 0.18 m/s), although it was only weakly constrained by the QRS. These results support the inclusion of image-derived fibrosis in reduced-order cardiac digital twins, and motivate an evaluation on a larger cohort to establish how consistently the improvement holds and to better analyze the role of the fibrotic

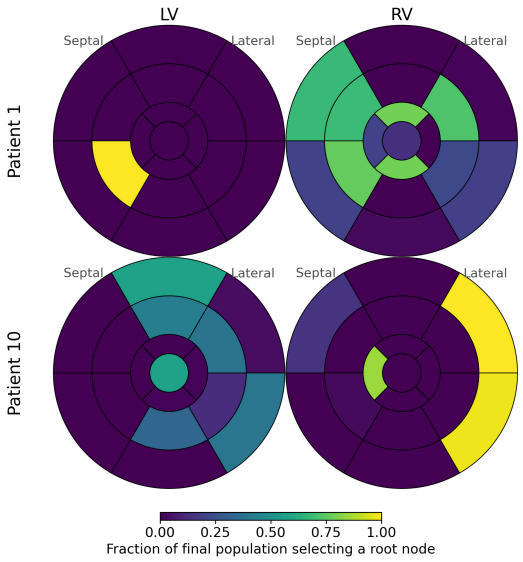

Figure 3: AHA bullseye of the fraction of the final population selecting a root node in each segment (LV and RV). The 17-segment model is applied to both ventricles through the biventricular coordinates; right-ventricular sectors follow the left-ventricular convention.

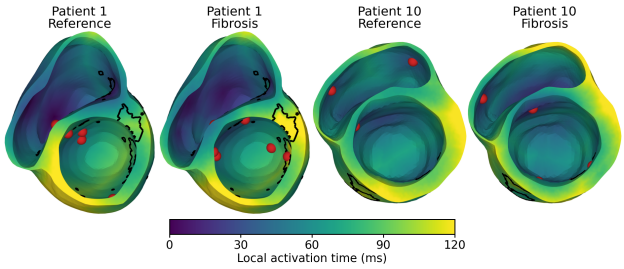

Figure 4: Local activation time maps for Patients 1 and 10 without and with explicit fibrosis, viewed from the base. Black contours mark where the segmented fibrotic region meets the rendered surface, so the enclosed area understates its true extent; red spheres are the root nodes of the corresponding inference. The colour scale is shared across all panels.

conduction velocity in these scenarios.

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