

Dyssynchrony without dysfunction: Left bundle branch block does not acutely reduce cardiac output

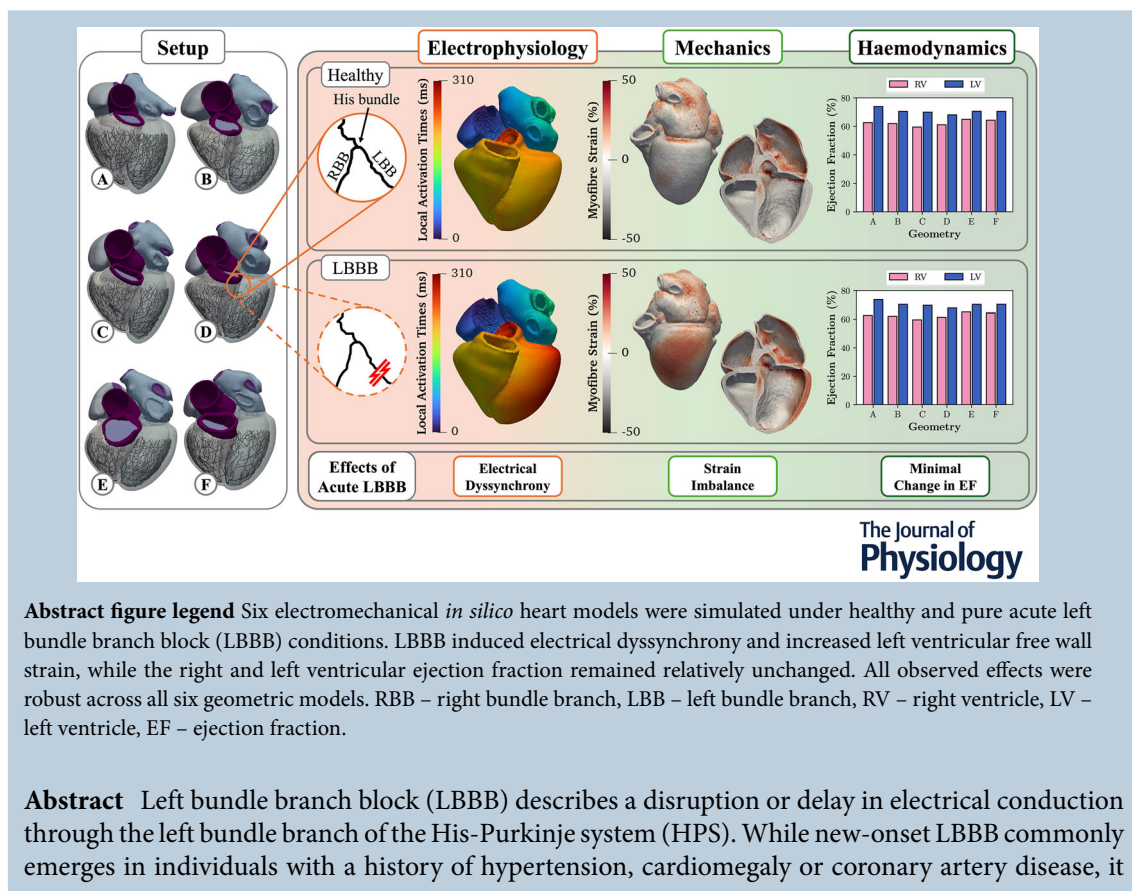
Carola Kruthoff¹ , Jonathan Krauß¹ , Jorge Sánchez², Tobias Gerach¹ , Cristian Barrios Espinosa¹ , Jan-Erik Duhme¹ and Axel Loewe¹ 

¹Institute of Biomedical Engineering, Karlsruhe Institute of Technology (KIT), Karlsruhe, Germany

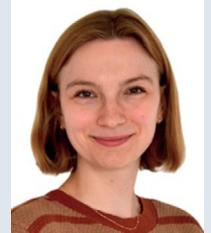
²Centro de Investigación e Innovación en Bioingeniería, Universitat Politècnica de València, Valencia, Spain

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Carola Kruthoff is a PhD candidate and research assistant at the Institute of Biomedical Engineering (IBT) of the Karlsruhe Institute of Technology (KIT). Her research focuses on electromechanical whole-heart modelling to investigate the mechanisms underlying complex cardiac diseases. Supervised by Dr Axel Loewe, she aims to unravel the pathomechanisms contributing to critical cardiac conditions such as dyssynchronous heart failure, hypertrophic cardiomyopathy and Takotsubo cardiomyopathy.



can also occur in the absence of other cardiovascular abnormalities. Whether LBBB is a cause or a consequence of heart failure remains unclear. In this work, we used six different electromechanical *in silico* heart models with an integrated HPS to simulate both a healthy control and a pure LBBB case for each geometry, affecting only the HPS in the absence of other cardiovascular pathologies. We compared electrophysiological, mechanical and haemodynamic metrics between both cases. Despite exhibiting a severe delay of up to 87 ms in left ventricular activation, all six virtual patients showed almost no acute change in ejection fraction (EF) due to LBBB. However, an absolute increase in septal flash of 1.4 mm to 2.7 mm indicated mechanical dyssynchrony. Furthermore, we observed a relative strain increase of 12.3–30% in the left ventricular free wall across all models. The load imbalance marked by the strain increase could drive LBBB-induced remodelling, leading to a major reduction in EF over time. Regardless of variations in heart geometry, this study shows that electrical dyssynchrony immediately affects mechanics more than haemodynamics. In line with clinical data, our findings suggest that patients with LBBB might benefit from an earlier application of cardiac resynchronization therapy to prevent strain-induced remodelling and preserve cardiac output.

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Corresponding author A. Loewe: Institute of Biomedical Engineering, Karlsruhe Institute of Technology (KIT), Karlsruhe, Germany. Email: publications@ibt.kit.edu

Key points

- Left bundle branch block (LBBB) describes an impairment of electrical conduction in the left bundle branch of the His-Purkinje system, causing a delay in left ventricular activation.
- While LBBB has been discussed as a risk factor for the progression of heart failure, the exact relationship of acute and chronic effects of LBBB in heart failure is not fully understood.
- In this study, we simulated both a healthy and a pure and acute LBBB scenario in six different electromechanical *in silico* heart models.
- Pure LBBB induced mechanical dyssynchrony, increasing septal flash and left ventricular free wall strain, while the ejection fraction remained virtually unchanged.
- The strain-induced load imbalance may cause long-term remodelling, reducing ejection fraction over time.
- In line with clinical data, our results suggest an early application of cardiac resynchronization therapy in patients with LBBB to prevent remodelling and sustain cardiac output.

Introduction

Left bundle branch block (LBBB) is characterized by an impairment of electrical conduction in the left bundle branch of the His-Purkinje system (HPS). This conduction abnormality results in delayed left ventricular activation. LBBB usually occurs alongside structural heart disease or degenerative changes, such as age-related fibrosis, Lev disease and Lenègre disease. However, LBBB can also emerge in the absence of other cardiovascular pathologies (Pérez-Riera et al., 2018).

In patients with pre-existing heart conditions, LBBB increases morbidity and mortality. It has also been hypothesized that the dyssynchronous electrical activation following LBBB by itself could be a cause of heart failure (HF) (Zannad et al., 2007).

One syndrome that often coincides with LBBB is dyssynchronous heart failure (HF_d). HF_d is characterized by an uncoordinated contraction of the ventricles and a substantial loss in pump function. The delayed activation of the left ventricle (LV) following LBBB is a common cause of the uncoordinated contraction (Dikdan et al., 2022).

Cardiac resynchronization therapy (CRT) has proven to be an effective treatment for HF_d patients, with new variations, including conduction system pacing, emerging in recent years (Glikson et al., 2021). The goal of CRT is to improve cardiac output by artificially restoring electrical synchrony. However, about one third of patients undergoing CRT do not experience long-term benefits (Glikson et al., 2021). Predicting the long-term outcome of CRT remains challenging because there is an incomplete

understanding of the relationship between the acute and chronic effects of LBBB in HF_d.

One reason for this lack of understanding is the clinical constraints on measurable data. Invasive measurements (e.g. pressure) are generally performed only on patients with suspected or established disease. Meanwhile, non-invasive techniques like speckle tracking (e.g. strain) are still underutilized due to vendor and user-specific measurement variability (Thomas et al., 2026). Computational cardiac modelling and simulation have proven to be valuable tools for clinical research and practice (Loewe et al., 2025; Niederer et al., 2019), which can overcome some of those limitations and complement other model systems (Streckfuss-Bömeke et al., 2026).

This study builds on a pilot investigation comparing a healthy control with LBBB in a single virtual patient (Kruthoff et al., 2025). Based on that pilot study presented as a conference contribution with preliminary results and a narrow analysis, we extended the simulation study of healthy control and LBBB cases to electro-mechanical heart models of six individuals, derived from imaging data. The goal of this work is to study the mechanisms underlying the effects of LBBB on cardiac mechanics and haemodynamics as well as their anatomical generalizability in a comprehensive in-depth analysis.

Materials and methods

Preprocessing heart geometries

We used six different geometries from the Rodero et al. cohort of adult healthy four-chamber heart geometries (Rodero et al., 2021a, 2021b). We refer to the individuals using the identifiers A–F. Patient characteristics are given in Table A1. In the following, the term ‘geometry’ will refer to a specific anatomical model.

The Rodero et al. cohort already provided segmentation labels for LV, right ventricle (RV), left atrium (LA), right atrium (RA), tricuspid valve, mitral valve, pulmonary valve, aortic valve, pulmonary veins, aorta, pulmonary artery and the orifices of the atrial cavities. To fulfil the requirements for the electrophysiology simulations and the mechanics and haemodynamics simulations, respectively, we generated an electrophysiology and a mechanics and haemodynamics version of each geometry. The characteristics of both versions are detailed below. A graphical overview of the complete preprocessing pipeline is shown in Fig. 1.

Electrophysiology geometries. All electrophysiology geometries were remeshed to a mean edge length of 0.44 mm. The geometries consisted only of the myocardium forming LV, RV, LA and RA. In contrast to the original geometries, valves and vessel trunks were omitted

for the electrophysiology simulations. The myocardium was further subdivided to capture fast-conducting bundles, the sinoatrial node and the coronary sinus in the atria. In the ventricles, we used the consistent biventricular coordinate system (CobivecoX) (Schuler et al., 2021; Pankewitz et al., 2024) to specify transmural heterogeneity. The thresholds used to define the three different regions (subendocardium, mid-myocardium, subepicardium) are given in Table A2. Ventricular fibre orientation was already assigned by Rodero et al. according to rule-based methods (Bayer et al., 2012). Atrial regions and fibre orientations were assigned using AugmentA (Azzolin et al., 2023).

All electrophysiology geometries included an explicit model of the HPS. We generated the HPS individually for each virtual patient utilizing anatomical landmarks to create the main branches and sites of earliest activation to guide the fractal growth (Correas et al., 2023). Both anatomical landmarks and sites of earliest activation were given in consistent biventricular coordinates (Schuler et al., 2021; Pankewitz et al., 2024). To model LBBB, we set the conductivity of a segment consisting of 21 line elements in the left bundle branch to a very low value (1×10^{-32} S/m). The LBBB segment was chosen manually for each geometry in the proximal part of the left bundle branch before it separates into anterior and posterior fascicles. For geometry A, the LBBB is visualized in Fig. 2.

Mechanics and haemodynamics geometries. The mechanics and haemodynamics geometries were remeshed to a mean edge length of 2.6 mm. For the mechanics and haemodynamics simulations the geometries incorporated all parts of the original models, including the myocardium of the four chambers as well as the valves and major-vessel trunks. Additionally, we generated a pericardium as a convex hull for each geometry to model a natural restriction of the heart's movement (Fritz, 2015; Krauß et al., 2023).

Simulation setup

We used a split simulation process. The electrophysiology simulations were performed with openCARP (Plank et al., 2021), whereas mechanics and haemodynamics were computed with CardioMechanics (Gerach, Fritz et al., 2023). Electromechanical coupling was achieved through the local activation times (LATs), which were computed in the openCARP simulation and subsequently used as input to the CardioMechanics simulation to trigger myocardial contraction. The LATs from the healthy atria were required to achieve a realistic simulation of the hearts' movement during a full cardiac cycle. The model of the pericardium restricts the movement of the whole heart and without the atria, one would, for example, neglect the

effect of the ventricles being stretched prior to their own contraction. A complete summary of the study setup is depicted in Fig. 3.

Electrophysiology simulation. The electrical activation was modelled with monodomain simulations using a timestep of 10 μ s. We obtained transmembrane voltages (V_m) as an output and computed the LAT of each node as the time at which V_m crossed a threshold of -50 mV with a positive slope.

In the atria, we used the Courtemanche et al. (1998) cell model with variations for the general myocardium, crista terminalis, pectinate muscles and interatrial connections (Bachmann's bundle, posterior, anterior and coronary sinus bridge). For the ventricles, we used the Tomek et al. (2019) cell model with variations for the subendocardial myocardium, the mid-myocardium and the subepicardial myocardium. The HPS cells were represented by the Stewart et al. (2009) model.

The HPS network was embedded in the subendocardial layer with all network elements isolated from the myocardium. The only connection between HPS and myocardium were the Purkinje-muscle junctions (PMJs): Each end of the network was connected to 30 nodes in the myocardium via a resistive element (R_m) (Vigmond & Clements, 2007). In our setup, the resistive element was calibrated to $R_m = 3$ k Ω . Coupling between the nodes in the HPS and the nodes in the myocardium at each PMJ was realized via coupling currents (I_{coupling}). The currents applied on myocardial and HPS nodes were calculated with the following formula in which N denotes the group size (myocardial nodes $N = 30$, HPS nodes $N = 1$).

$$I_{\text{coupling}} = \sum_{i=1}^N \frac{1}{R_m} \left(V_m \left(x_{\text{hps}}^{\text{pmj}} \right) - V_m \left(x_{\text{myo},i}^{\text{pmj}} \right) \right) \quad (1)$$

All cell models were paced to a limit cycle at a heart rate of 60 bpm in single cell simulations. The limit cycle refers to the state variables reaching a stable periodic

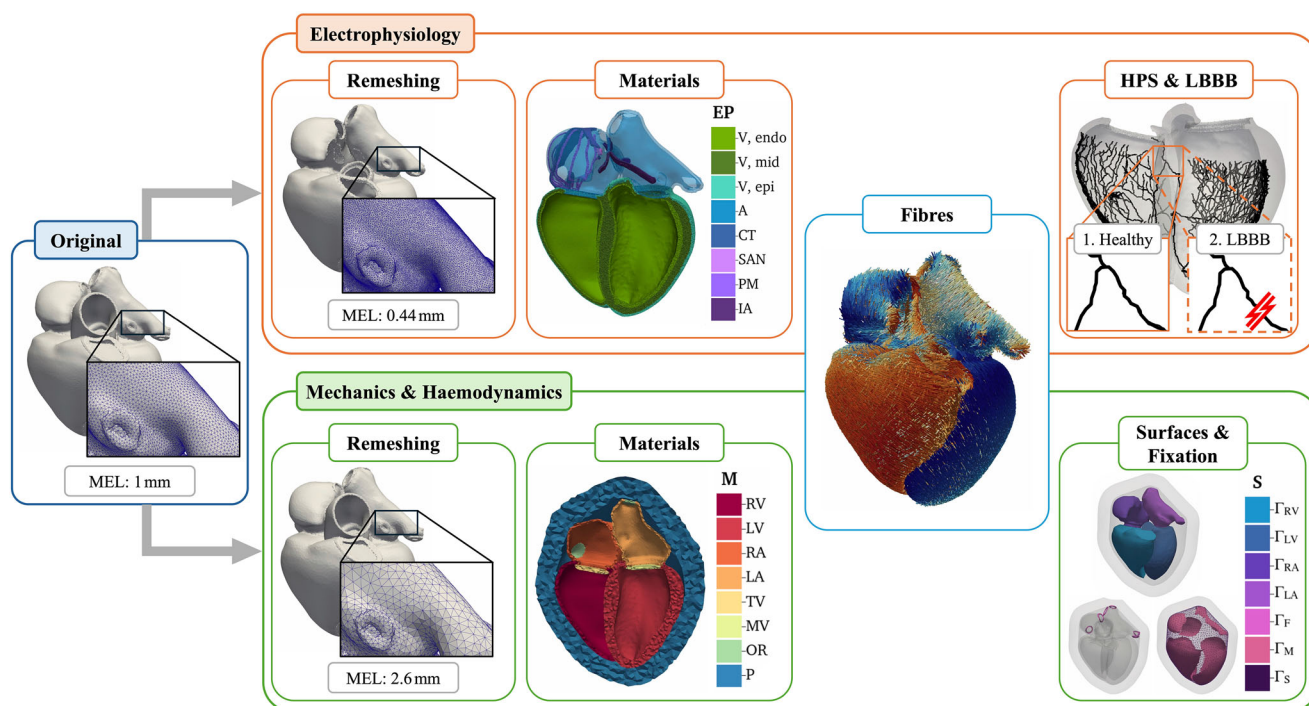


Figure 1. Graphical summary of the preprocessing pipeline

The original geometry with a mean edge length of approx. 1 mm was remeshed to a fine and a coarse geometry for electrophysiology and mechanics, respectively. The electrophysiology geometry consisted solely of the myocardium of the four chambers, while the mechanics and haemodynamics geometry included vessel trunks and an artificially generated pericardium. Different materials were assigned to depict varying electrophysiological and mechanical characteristics. Fibre directions were the same for both geometries. Finally, the His-Purkinje system (HPS) for the electrophysiology geometry was generated – with and without left bundle branch block (LBBB). Both scenarios are illustrated in the insets in the upper right panel. The right inset marks the position of the LBBB using a red bolt-like symbol. The last step for the mechanics and haemodynamics geometry was the creation of surfaces for the four chambers (Γ_{RV} , Γ_{LV} , Γ_{RA} , Γ_{LA}), the fixed rings around the orifices (Γ_F) and the contact problem (Γ_M , Γ_S). While the images depict geometry A, the pipeline applies for all geometries. V – ventricles, A – atria, CT – crista terminalis, PM – pectinate muscle, IA – interatrial connections, TV – tricuspid valve, MV – mitral valve, OR – orifices, P – Pericardium.

Table 1. Conduction velocities (CVs) in m/s for the ventricles and different atrial regions. Atrial CVs were based on (Loewe, 2016), ventricular CVs were based on (Fu et al., 2024).

Region	Longitudinal	Transversal	Normal
Atrial myocardium	1.0	0.515	
Crista terminalis	1.320	0.515	
Pectinate muscles	1.358	0.419	
Interatrial connections	1.666	0.555	
Ventricles	0.8	0.3	0.2

Table 2. Monodomain conductivities in S/m for the different atrial regions, the ventricles and the His-Purkinje system.

Region	Longitudinal	Transversal	Normal
Atrial myocardium	0.4722	0.1615	
Crista terminalis	0.7548	0.1612	
Pectinate muscles	0.7919	0.1176	
Interatrial connections	1.0989	0.1812	
Ventricles	0.2657	0.0613	0.0366
HPS		12.15	
Left bundle branch block		10^{-32}	

trajectory. The tissue conductivities for all atrial and ventricular regions were obtained by tuning for physiological conduction velocities (CVs) (Costa et al., 2013) from literature (Table 1). The conductivity of the HPS was adopted from our pilot study (Kruthoff et al., 2025). All final conductivities are listed in Table 2.

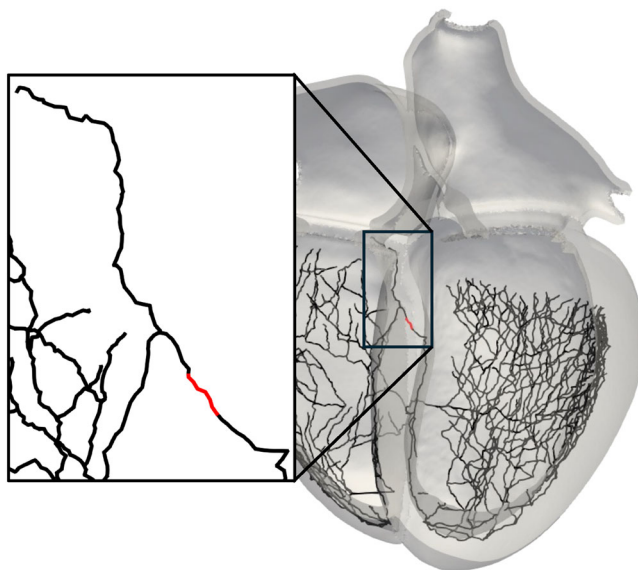


Figure 2. His-Purkinje system with LBBB and whole-heart geometry A

Inset: Area of the left bundle branch block highlighted in red.

To initiate electrical activation, the atria and the ventricles were stimulated sequentially. In the atria, we applied a stimulus in the region representing the sinoatrial node. In the ventricles, we considered the start of the HPS as the atrioventricular node and stimulated it with a delay of 150 ms to the sinoatrial node. Both stimuli had an amplitude of $200 \mu\text{A}/\text{cm}^3$ and lasted 2 ms. We simulated every case for three heartbeats and only analysed the last one to minimize the influence of drifting. A limit cycle was reached after two beats.

Mechanics and haemodynamics simulation. The mechanics simulations employed the tension model by Niederer et al. (2011). The parametrization of the tension model was adopted from Gerach, Schuler et al. (2023). To fit our heart rate of 60 bpm, we reduced the time constants to approximately 80% of their original values. All parameters of the active tension model are displayed in Table A3. The passive material properties of the myocardium were modelled with the hyperelastic strain energy function by Usyk et al. (2000). All material properties of the myocardium used for all geometries are displayed in Table A4. Other geometry components (valves, vessel trunks, orifices and pericardium) were modelled as an isotropic NeoHookean material (Table A5).

To simultaneously estimate a stress-free reference configuration and optimize passive material properties for each geometry, we used the method proposed by Marx et al. (2022). Following this, the parameters for the constitutive model were chosen for the end diastolic pressure–volume relationship of the LV matching the data by Klotz et al. (2006). The initial values for this optimization were taken from Gerach and Loewe (2024). The dataset from Rodero et al. (2021a) did not include invasive pressure measurements. Therefore, we assumed diastolic pressures to be $p_{t=0,RV} = 3.75 \text{ mmHg}$, $p_{t=0,RA} = 4.5 \text{ mmHg}$, $p_{t=0,LV} = 7.4 \text{ mmHg}$, and $p_{t=0,LA} = 8.25 \text{ mmHg}$, in accordance with Gerach and Loewe (2024). The geometry-specific scaling parameters of the tissue stiffness obtained through this procedure are documented in Table A6.

Haemodynamics were modelled with a 0D closed-looped model, including a three-element Windkessel model each to represent the systemic and pulmonary circulation. This circulatory system model was coupled to the mechanics to guarantee volume consistency between the 3D and 0D models (Gerach, Krauss et al., 2023). The haemodynamics simulations compute continuous data on the pressure and volume in all four chambers.

The LATs from the electrophysiology simulation were mapped to the mechanics geometry and served as an input to the active tension model, initiating contraction onset. To let drifting effects stabilize, we performed the

mechanics and haemodynamics simulation for five beats and analysed the last one.

Analysis metrics

We employed different analysis metrics to evaluate the variance between the six virtual patients and their two cases (healthy control and LBBB).

To quantify electrical dyssynchrony, we computed dyssynchrony indices as proposed by Ploux et al. (2015):

- Total activation time (TAT): Time difference between earliest and latest site of activation, calculated for both ventricles and for each ventricle individually.
- Ventricular uncoupling (VEU): mean activation time of LV – mean activation time of RV.

To visualize the spatial distribution of the activation times, we used a biventricular bullseye plot. The LV was divided according to the 17 American Heart Association segments (Cerqueira et al., 2002). The RV was segmented in a similar manner. The basal and mid segments of the RV were computed according to the same metrics used for the LV, excluding the segments that belong to the septum. The apical ring was divided into four segments equal to the basal and mid ring. Additionally, we dedicated one

segment to the apex. The resulting segmentation is shown in Fig. 4.

To analyse mechanical function, we focused on three areas in the ventricles: the right ventricular free wall (RVfw), the septum and the left ventricular free wall (LVfw). For all three areas we chose the lateral segments in the bullseye plots and cut off the top part of the base. Hence, these areas were composed of the following segments:

- RVfw: 19, 20, 23, 24, 27, 28
- Septum: 2, 3, 8, 9, 14
- LVfw: 5, 6, 11, 12, 16

Septal flash (SF) is a clinically used marker of mechanical dyssynchrony (Calle et al., 2020). This marker is defined as the extent of the septum's subsequent leftward movement toward the LV epicardium, following its initial rightward motion after the onset of ventricular excitation. To measure SF, we mimicked ultrasound M-mode tracking, as proposed by Walmsley et al. (2015). For this purpose, we manually placed a line through the middle of the LVfw and the septum. To visualize the movement of the LVfw and the septum, we tracked the points on the epi- and endocardium closest to this line. This process is illustrated in Fig. 5.

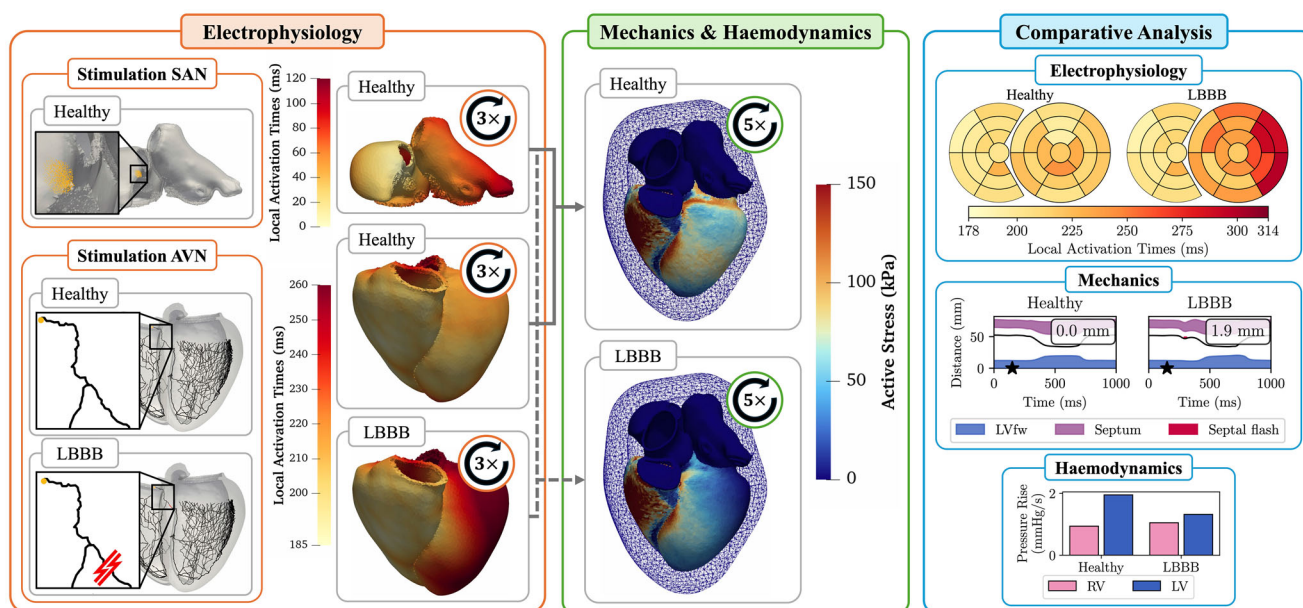


Figure 3. Graphical overview of the study setup

Electrical activation was initiated by stimulating the sinoatrial node (SAN) in the atria and the atrioventricular node (AVN) in the ventricles. The healthy atria were simulated separately from the two ventricle simulations (healthy control vs. left bundle branch block (LBBB) case). All electrophysiology simulations ran for three beats (3x). Local activation times from the third beat were mapped to the mechanics and haemodynamics geometry to simulate cardiac contraction for the healthy control and the LBBB case. Both mechanics and haemodynamics simulations used the same activation times from the healthy atria and ran for five beats (5x). Finally, electrophysiological, mechanical and haemodynamic readouts were compared across all geometries, using the results from the final heartbeat. While the images depict geometry A, the pipeline applies for all geometries.

To evaluate the load on the lateral walls of the ventricles, we analysed the myofibre strain over time for the RVfw, septum and LVfw. In addition to the myofibre strain, we used the local deformation energy, to quantify the load on the ventricles globally. The local deformation energy is derived from the strain energy function Ψ defined by the material model for each volume element at every time step. We visualized this metric on the biventricular bullseye plot in a multistep process. First, we summed up the deformation energy across all volume elements within each of the 30 segments (Fig. 4) and normalized it by the segment volume to obtain the deformation energy density (DED) for each segment. This calculation was done for all time steps, yielding a time-dependent DED curve for each segment. Next, we computed the mean DED value over all time steps for each segment. Finally, we calculated the relative difference in mean DED between the healthy control and LBBB cases as follows: $(\text{mean DED(Healthy)} - \text{mean DED(LBBB)})/\text{mean DED(Healthy)}$.

Haemodynamic analysis was performed with clinically established metrics relevant to the assessment of LBBB (Niederer et al., 2011). Using the continuous pressure and volume data, we obtained the end diastolic volume (EDV) and the end systolic volume (ESV) and calculated the ejection fraction ($EF = \frac{EDV - ESV}{EDV}$). We computed the maximum rate of systolic pressure rise ($dp/dt_{\max}$), since it is used as an indication for the response to CRT (Ploux et al., 2015) and as an expression of myocardial contra-

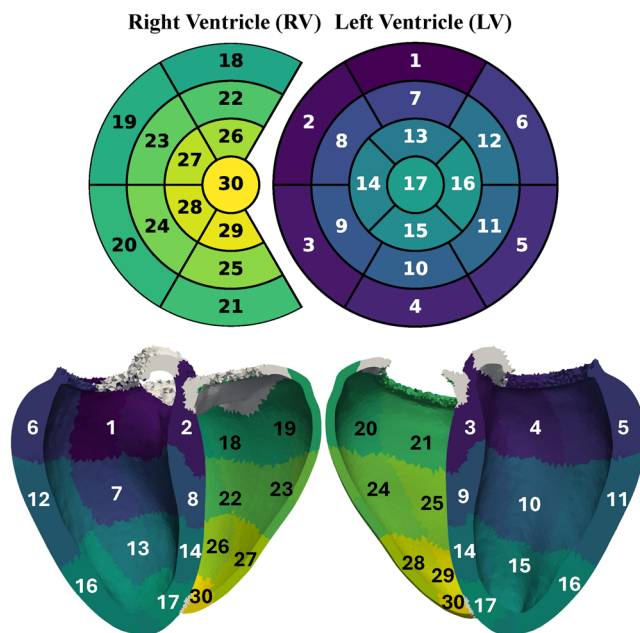


Figure 4. Modified American Heart Association segmentation of both ventricles for geometry A

Top: Bullseye plot of all segments. Bottom: segmentation on the 3D biventricular geometry. Parts in light grey are not assigned to any segment.

Table 3. Septal flash in mm measured via pseudo M-mode.

Geometry	Healthy	LBBB
A	0.0	1.9
B	0.2	1.6
C	0.5	3.2
D	2.1	3.9
E	0.1	2.3
F	0.0	2.3

tility (Hamlin & Del Rio, 2012). Finally, we plotted the pressure–volume loops (pV loops) to visualize the overall changes in pressure and volume for the RV and LV.

Results

For all results, we analysed a full heart cycle, starting with the activation of the sinoatrial node. With a heart rate of 60 bpm, one heart cycle has a length of 1000 ms with the activation of the sinoatrial node starting at 0 ms and the activation of the atrioventricular node (AVN) at 150 ms. We marked the AVN activation with a black star on the time axis of the pseudo M-mode and the strain plots.

Electrophysiology

Activation was prolonged in the LV for the LBBB case for all six geometries (Fig. 6). This prolongation was especially pronounced in the lateral segments of the LV but appeared in the radial segments and the septum as well.

This electrical dyssynchrony is also evident in the TATs and the ventricular uncoupling (VEU) (Fig. 7). In LBBB, the TAT of the RV was elevated with up to 14 ms, while the TAT for both ventricles and the LV showed greater augmentations of up to 52 ms compared with the healthy case. The VEU with LBBB was elevated for all geometries, with absolute differences from the healthy case ranging between 32 and 38 ms.

Mechanics

An exemplary pseudo M-mode with calculation of the SF for geometry A is shown in Fig. 8. The pseudo M-mode images of the remaining five geometries demonstrate the variance of chamber size and wall thickness (Fig. A1). Independent of the healthy SF ranging from 0.0 mm to 2.1 mm, all virtual patients experienced a substantial increase in SF for the LBBB case, with absolute differences varying between 1.4 mm and 2.7 mm (Table 3).

Mechanical dyssynchrony also became evident in the myofibre strain (Fig. 9). In the RVfw, we saw a slight increase in strain for the LBBB case at the end of systole

(approximately 750 ms). In the septum, the strain curve for LBBB was shifted slightly to the right due to the occurring activation delay. The myofibre strain in the LVfw exhibited the most drastic change due to LBBB with a sizeable increase in strain at approximately 350 ms. The absolute difference between the maximum strain in the healthy and the LBBB case ranged between 2.3% and 4.2%. As a relative difference normalized to the healthy control maximum values, this constitutes 12.3–30%. The absolute maximum strain values are displayed in Table A7.

This imbalanced load on the myocardium was also reflected in the DED (Fig. 10). The relative difference in mean DED between the two cases revealed an increase for the LBBB case especially in the lateral segments of the LV (up to 21.3 %). For LBBB, the DED in the LV apex and some segments of the septum showed a reduction of up to −4.1 %. In the RV, we saw a slight increase in DED (up to 4.3 %) or no change compared with the healthy case.

Haemodynamics

Relative changes in EF were limited to less than 1% for all geometries. While the right ventricular ejection fraction increased slightly for all six geometries, the left ventricular ejection fraction (LVEF) decreased because of LBBB (Fig. 11). Changes in stroke volume also stayed under 1 mL. Absolute values in EF and stroke volume are displayed in Table A8 and Table A9, respectively.

The changes in maximum rate of systolic pressure rise ($dp/dt_{\max}$) were more pronounced (Fig. 11). $dp/dt_{\max}$ showed a relative decrease between −6.1% and −10.9% and −18.9% and −39.7% in the RV and LV, respectively. Geometry E exhibited deviating behaviour with $dp/dt_{\max}$

in the RV experiencing a relative increase of 1%. Absolute values for $dp/dt_{\max}$ are displayed in Table A10.

The pressure–volume loops (pV loops) showed a decrease in area enclosed by the pV loop for the LV, while the area inside the RV pV loop slightly increased in the LBBB scenario (Fig. 12). These changes in area size are mainly caused by variations in minimal and maximum pressure.

Discussion

Our pilot study (Kruthoff et al., 2025) showed that the onset of pure LBBB causes electrical and mechanical dyssynchrony but does not lead to an immediate, severe reduction in pump function. The current work provides additional insight into the spatial manifestation of the activation time delay and the specific mechanisms behind the increased mechanical load caused by LBBB. It further demonstrates that despite differences in anatomical structures among the subjects, the key electrical, mechanical and haemodynamic outcomes remained consistent. This suggests that the observed phenomena are intrinsic to the underlying pathological mechanisms following LBBB rather than being influenced by inter-subject geometric variability.

We observed only minimal immediate changes in EF and stroke volume but a marked instant decrease in $dp/dt_{\max}$ for the LBBB case across all virtual patients. The systolic pressure rise (dp/dt) is usually the steepest during the beginning of ventricular contraction, while both valves are still closed for the right and left ventricle. In the case of LBBB, the ventricles start contracting with a slight delay to each other, so the pressure cannot rise as fast as it

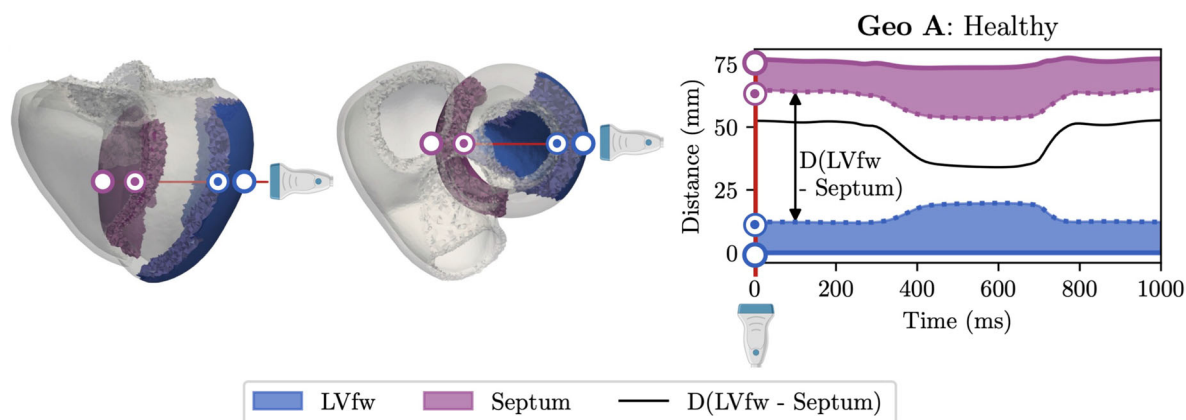


Figure 5. Visual explanation of the creation of a pseudo M-mode image using geometry A

Left: The red line imitates the field of view of an ultrasound probe. The blue and violet points mark the tracked points on the epi- and endocardium of the left ventricular free wall (LVfw) and the septum, respectively. *Right:* An exemplary pseudo M-mode is shown, with the blue and violet points on the y-axis corresponding to the points on the biventricular geometry in the left panel. The black line indicates the distance between the endocardium of the LVfw and the septum. Time 0 ms corresponds to the activation of the sinoatrial node. Image of the ultrasound probe from BioRender.

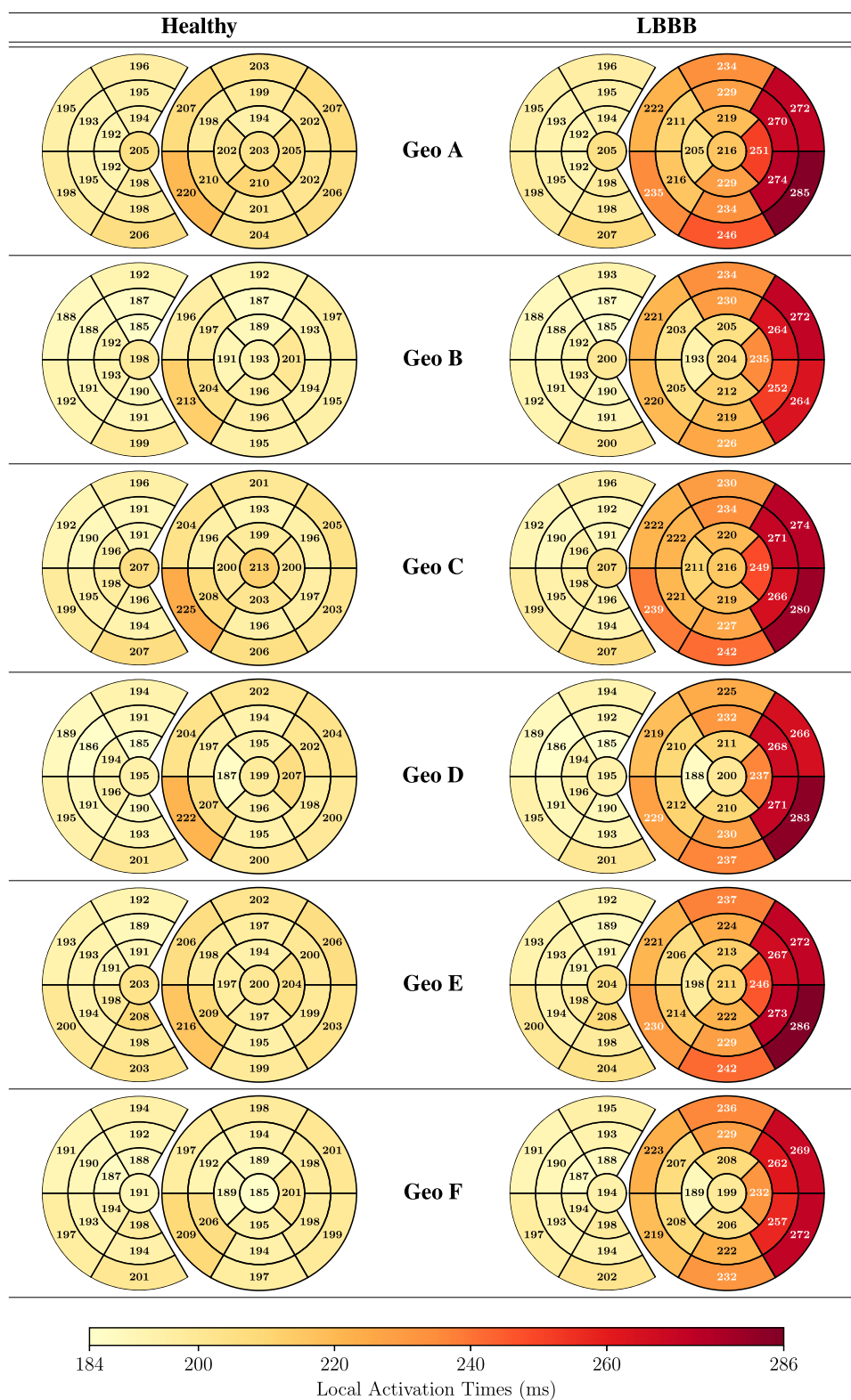
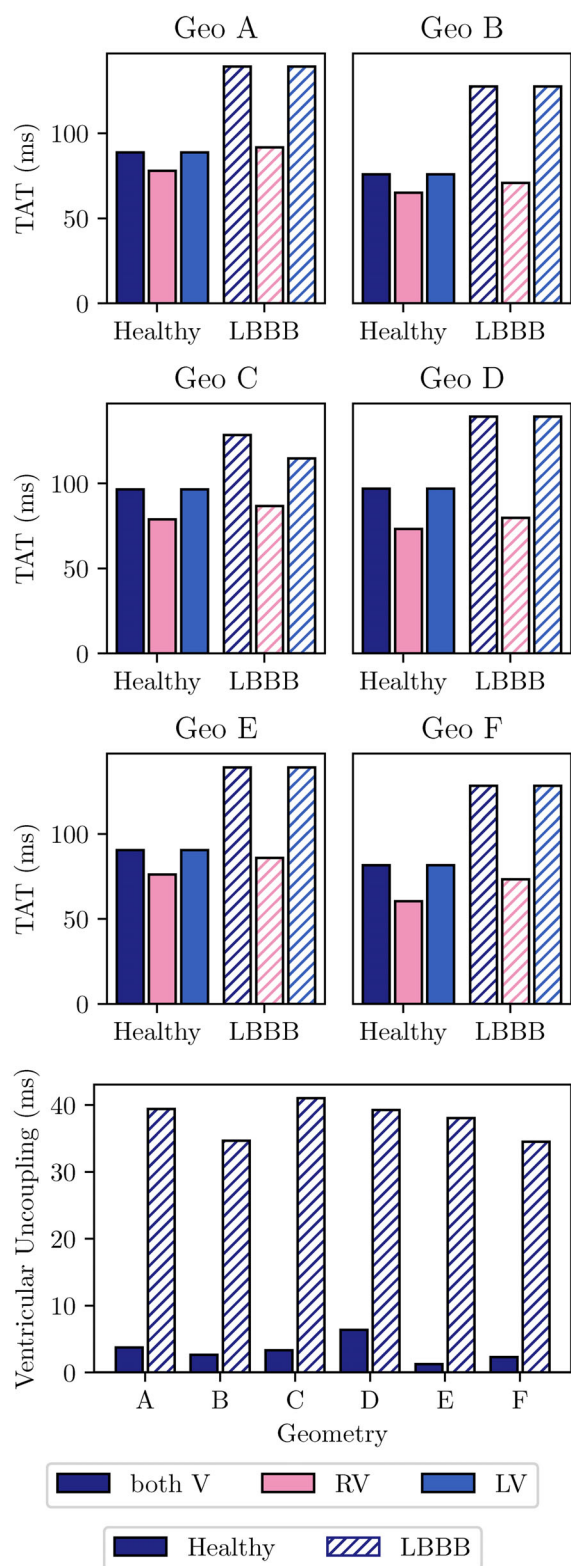


Figure 6. Local activation times of the ventricles in bullseye plot representation for the healthy control and the left bundle branch block (LBBB) cases of each geometry.

**Figure 7.**

Top: Total activation times (TATs) for both ventricles (both V), the right ventricle (RV) and the left ventricle (LV) for the healthy control and left bundle branch block (LBBB) case for each geometry. *Bottom:* Ventricular uncoupling for the healthy and LBBB case for each geometry.

would with a synchronous contraction. While $dp/dt_{\max}$ in both ventricles drops by up to 39.7%, the peak systolic pressure decreases by only 3.1–6.3% (Table A11). This decrease in peak pressure can also be seen in the pV loops (Fig. 12), which demonstrate that both healthy and LBBB cases reached the same ESV, while EDV was only slightly decreased for the LBBB case. So even though the pressure rise is less steep, the systolic pressure remains sufficient to preserve a normal pump function even with LBBB.

Apart from the preserved EF, our simulations reproduced electrical and mechanical dyssynchrony as typical features of LBBB morphology (Pérez-Riera et al., 2018). Electrical dyssynchrony was caused by the electrical impulse reaching the LV from the RV myocardium instead of the left side of the HPS. This resulted in a 33.1–68.2% prolongation of ventricular TATs compared with healthy controls, which would correspond to the characteristic QRS widening observed in LBBB patients (Pérez-Riera et al., 2018). Variance in activation times and relative delay can be explained by the size differences between the different hearts.

Mechanical dyssynchrony was demonstrated by the increase in SF for LBBB. SF has been discussed as a predictor of CRT response (Dikdan et al., 2022), since an increase in SF is linked directly to the contraction onset in the RV preceding the contraction onset in the LV.

Geometry D stands out with a markedly elevated healthy SF compared with the other geometries. This anomaly demonstrates the natural variations created by patient-specific geometries as detailed in Appendix A.7.

The substantial augmentation in LVfw myofibre strain with the introduction of LBBB is also a direct consequence of mechanical dyssynchrony. The LV is still relaxed, while the RV starts contracting, which results in a circumferential stretch in the LVfw. The strain increase is visualized on the whole-heart geometry in Fig. 13. A clip through the long axis of the heart reveals the thinning of the LVfw for LBBB compared with the healthy control (Fig. 13).

This LBBB-induced load imbalance further manifests in the increased mean DED for the LV. With our findings showing a substantial increase in LV myofibre strain, it seems likely that the LV must summon more energy to contract, countering the stretch introduced by the early contraction from the RV. The decrease of DED in the apical region of the septum is likely due to a redistribution in deformation energy with the purpose of minimizing the total deformation energy. Additionally, the changes in LV pV loop area suggest a minor overall reduction in external mechanical work for the LV.

Considering the evident electrical and mechanical dyssynchrony, the absence of an acute change in cardiac output seems counterintuitive. In HF_d patients, LBBB often coincides with other conditions such as coronary artery disease, cardiomyopathies or age-related fibrosis.

These comorbidities can independently reduce EF. A study by Brunekreeft et al. (2007) examined HF_A patients with pure LBBB and found their average LVEFs to be significantly lower (approximately 44%) compared to healthy controls (approx. 63%). The data by Brunekreeft et al. (2007) raises the question, why there are almost no changes in cardiac output for our pure LBBB case.

This distinct preservation in pump function prompted us to critically assess our methodological setup. Our model, which has been verified and validated previously (Fritz, 2015; Land et al., 2017; Gerach et al., 2021), aligns with established approaches in the field (Augustin et al., 2016; Finsberg, 2019; Fedele et al., 2023; Aróstica et al., 2025; Al-Ali et al., 2026). The most relevant differences among these models are the representation of the effect of the pericardium by sliding contact vs. spring forces or Robin boundary conditions, use of different active stress models and the implementation of mechano-electrical feedback.

Krauß et al. (2023) compared different approaches for modelling the restraining effect of the pericardium. While all of them produced comparable results, the sliding contact formulation showed the best balance of accuracy and computational cost. In our pilot study (Kruthoff et al., 2025), we tested different active stress models and different parameterizations and found no significant impact on qualitative outcomes, thereby supporting the robustness of our findings.

We compared our findings with similar simulation scenarios with other heart models. Meiburg et al. (2023) used the CircAdapt model (Lumens et al., 2009) to simulate pacing strategies, assuming atrioventricular block for all scenarios. Their findings on right ventricular apex pacing and selective His-bundle pacing align with our LBBB and healthy case, respectively. They observed minor haemodynamic changes, with selective His-bundle

pacing showing a relative LVEF increase of $\approx 1.5\%$ over right ventricular apex pacing.

Similarly, Zingaro et al. (2024) found a 1.3% LVEF increase in a healthy case compared with LBBB using a multiphysics model. While these relative changes (1.3% to 1.5%) exceed our observed reductions, they remain far below the $\approx 30\%$ reduction seen clinically by Brunekreeft et al. (2007).

The works by Meiburg et al. and Zingaro et al. also confirm our findings of emerging mechanical dyssynchrony together with a load imbalance regardless of specific modelling choices. The CircAdapt model (Lumens et al., 2009) used by Meiburg et al. (2023) divides the ventricles into a limited number of patches and determines the wall tension based on the area of these patches. Their LBBB-equivalent simulation showed a major increase in LVfw strain, as well as an increase in myocardial work density in the lateral segments of the LV compared with their healthy-equivalent simulation. Zingaro et al. (2024) modelled mechanical activation using the RDQ20 active contraction model and included the effect of mechano-electric feedback. They noticed an abnormal leftward motion of the septum due to LBBB – corresponding to our SF.

Simulations like the ones presented here and those by Meiburg et al. (2023) or Zingaro et al. (2024) model purely acute effects of the applied conditions. Especially in our case with heart geometries from healthy individuals and a healthy parametrization, the simulations only depict the acute impact of LBBB right after its onset. The patients from Brunekreeft et al. (2007) could be suffering from LBBB for an extended period of time.

In a healthy heart with healthy tissue and a low heart rate, both ventricles are still able to reach a state of full contraction equivalent to the healthy scenario (Fig. 14), resulting in an almost full preservation of

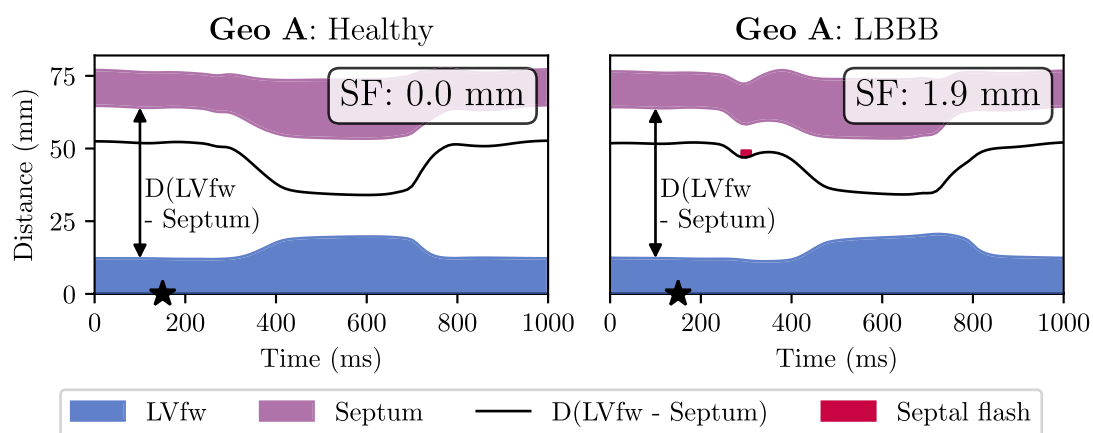


Figure 8. Pseudo M-mode of geometry A for the healthy and the left bundle branch block (LBBB) case
D(LVfw–Septum) is the distance difference between the left ventricular free wall (LVfw) endocardium and the septal endocardium, with both distances measured from the LVfw epicardium. The activation of the atrioventricular node is marked with a black star.

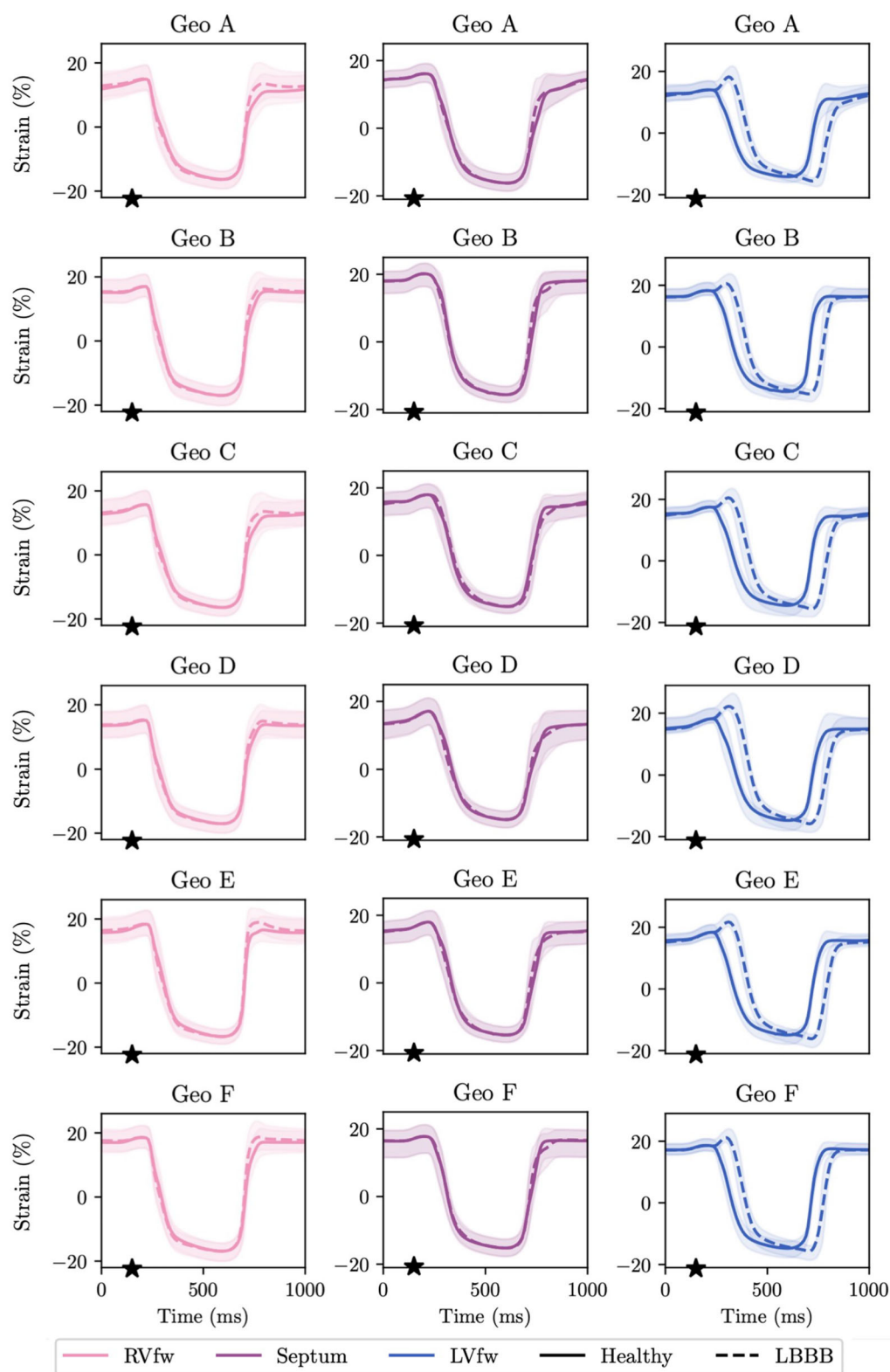


Figure 9. Myofibre strain over one heartbeat in the right ventricular free wall (RVfw), septum and left ventricular free wall (LVfw), for the healthy and the left bundle branch block (LBBB) cases

Lines show the mean value, shaded areas represent interquartile range. The activation of the atrioventricular node is marked with a black star.

LVEF. Additional mechanistic insight into the effects contributing to LVEF preservation are given in Appendix A.8.

Considering the observed strain increase creating a load imbalance on the ventricles, we hypothesize that the severe pump function decrease seen in HF_d patients with LBBB is primarily a result of remodelling over time. The following clinical studies on the acute effects of pure LBBB support this hypothesis.

Vaillant et al. (2013) retrospectively examined 375 patients with pure LBBB and a LVEF > 50% at the diagnosis of LBBB. All patients developed symptoms consistent with HF within a mean of 11.6 years after their LBBB diagnosis. Their LVEF progressively decreased to ≤40% during this time, finally resulting in an indication for CRT.

Wiedmann et al. (2024) used a porcine large-animal model to induce LBBB via radiofrequency ablation. They documented the state of the pigs directly before and after

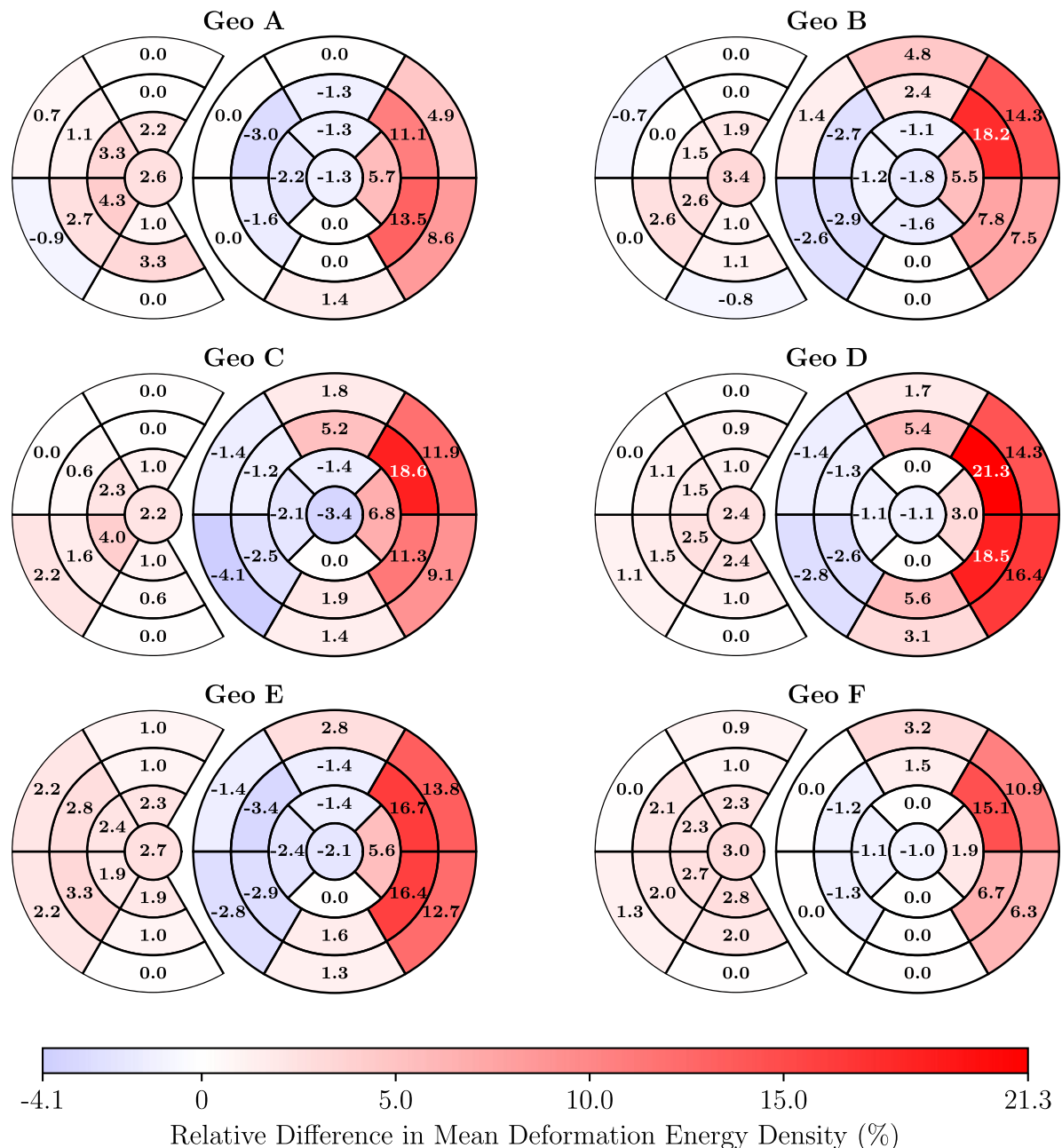


Figure 10. Relative differences in mean deformation energy density (DED) between the healthy and the left bundle branch block (LBBB) case for all geometries
The relative difference is calculated as follows: $(\text{mean DED(Healthy)} - \text{mean DED(LBBB)}) / \text{mean DED(Healthy)}$.

the ablation as well as seven and 21 days afterwards and introduced CRT in a subgroup of pigs at day seven. Following the implementation of LBBB, the QRS complex and the ventricular TAT was prolonged. Furthermore, a characteristic SF was apparent, while the LVEF remained unchanged in all animals over the complete three weeks of follow-up. The introduction of CRT was successful in shortening the QRS complex and resynchronizing the septal motion. These findings demonstrated all effects we saw in our *in silico* model in an *in vivo* large animal model.

Calle et al. (2021) differentiated between four stages of LBBB based on increasing severity of SF. Patients with

higher LBBB stages showed larger EDVs, lower ejection fractions, longer QRS duration and increased mechanical dyssynchrony compared with less severe stages. They also revealed that patients who were considered CRT super-responders experienced an inverse transition from LBBB stages 3 and 4 before the implant to stages 1 and 2 during a median follow-up of 66 months. The evolution of pump function in super-responders fortifies the notion, that change in pump function follows remodelling over time. Additionally, Calle et al. (2021) considered transcatheter aortic valve replacement (TAVR) patients with new-onset TAVR-induced LBBB 24 h post-TAVR. Based on their longitudinal septal strain pattern, 96% of patients in this group were categorized as LBBB stage ≤ 2 . No data on pre-TAVR LVEF are reported; the mean LVEF after TAVR-induced LBBB was 58%. These findings support our hypothesis that degenerative changes reduce the pump function over time. They also stress the importance of mechanical metrics like septal strain when predicting the risk of electrical dyssynchrony-induced future haemodynamic impairment.

Our mechanistic *in silico* findings, in line with clinical observations, provide potential implications for pacing therapies like CRT. So far, the acute indicators for a successful implementation of CRT are the width of the QRS complex (electrical resynchronization) (Abraham et al., 2002) and the change in LV $dp/dt_{\max}$ (Prinzen & Auricchio, 2012). Despite their clinical use, current selection criteria have limited predictive accuracy, as long-term response to treatment is observed in only approximately two-thirds of patients (Glikson et al., 2021).

A review by Prinzen and Auricchio (2012) concluded that CRT can achieve a long-term positive effect if it is associated with a reverse remodelling process. The review demonstrates that this reverse remodelling process is more likely driven by mechanical recoordination rather than an immediate haemodynamic response. Especially the normalization of strain appears to play a major role in the initiation of remodelling processes, in line with findings by Breithardt et al. (2003). While the review by Prinzen and Auricchio focused on electrical resynchronization (CRT) as a treatment for HF_d, our work considered electrical dyssynchrony as the root cause of HF_d, drawing similar conclusions. Based on our results and the findings from Prinzen and Auricchio (2012), we hypothesize that earlier application of CRT in patients with LBBB and only mildly reduced EF may prevent adverse remodelling.

This hypothesis is backed by a study by Wang et al. (2016). They showed that patients with LBBB generally did not respond to guideline-directed medical therapy. Instead, their LVEF degenerated over time during pharmaceutical treatment. Only after the implementation of CRT did they experience a substantial increase in pump function with 35% of patients reaching a LVEF > 50%, classifying as super-responders. An earlier application of

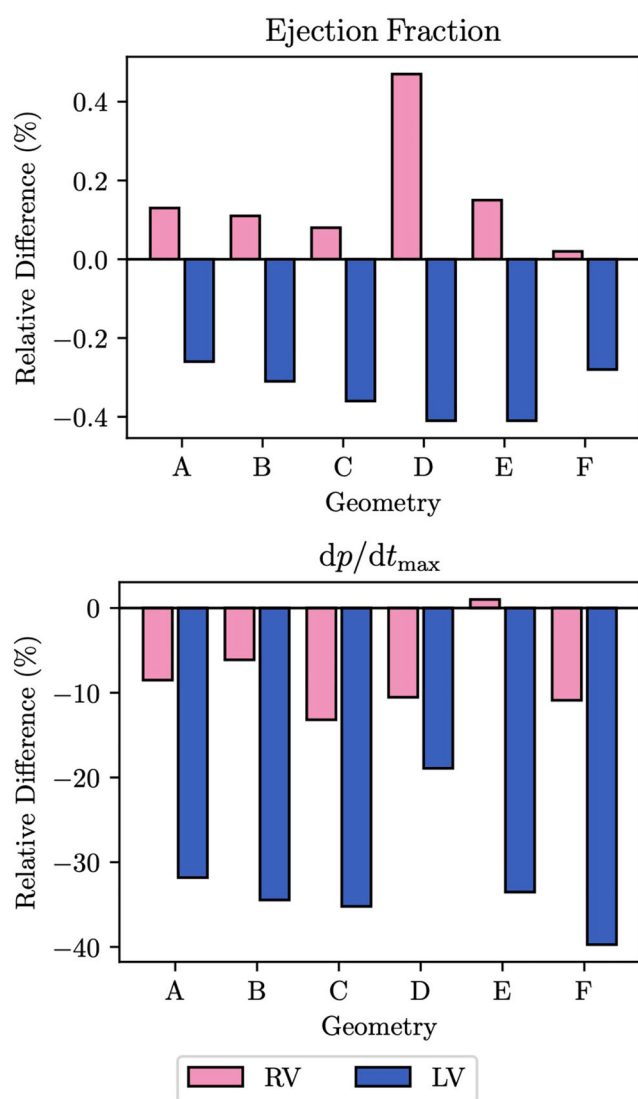


Figure 11. Relative difference in ejection fraction (EF) and maximum rate of systolic pressure rise ($dp/dt_{\max}$) between healthy and left bundle branch block (LBBB) cases for all geometries

The relative difference for ejection fraction (EF) and maximum rate of systolic pressure rise ($dp/dt_{\max}$) is calculated as follows: $(EF(\text{LBBB}) - EF(\text{Healthy})) / EF(\text{Healthy})$.

CRT in patients with LBBB is also recommended by Sze et al. (2017) and Sletten et al. (2021) with the objective of preventing left ventricular systolic dysfunction or remodelling and improving clinical outcomes.

Limitations

The main limitation of this study is the fact that structural remodelling or a long-term modulation of gene expression cannot be captured with our framework.

The uni-directional coupling between electrophysiology and mechanical simulations through

LATs enables the implementation of an explicit HPS representation but neglects the effects of mechano-electric feedback. Since strain and stretch play important roles in LBBB, we would expect the most prominent effect of mechano-electrical feedback to be caused by stretch-activated channels (Quinn & Kohl, 2021). However, their parametrization is highly uncertain (Gerach & Loewe, 2024), requiring additional experimental data before drawing conclusions from whole-heart *in silico* models that include them. Our results are consistent with clinical observations and comparable to those of Zingaro et al. (2024) who

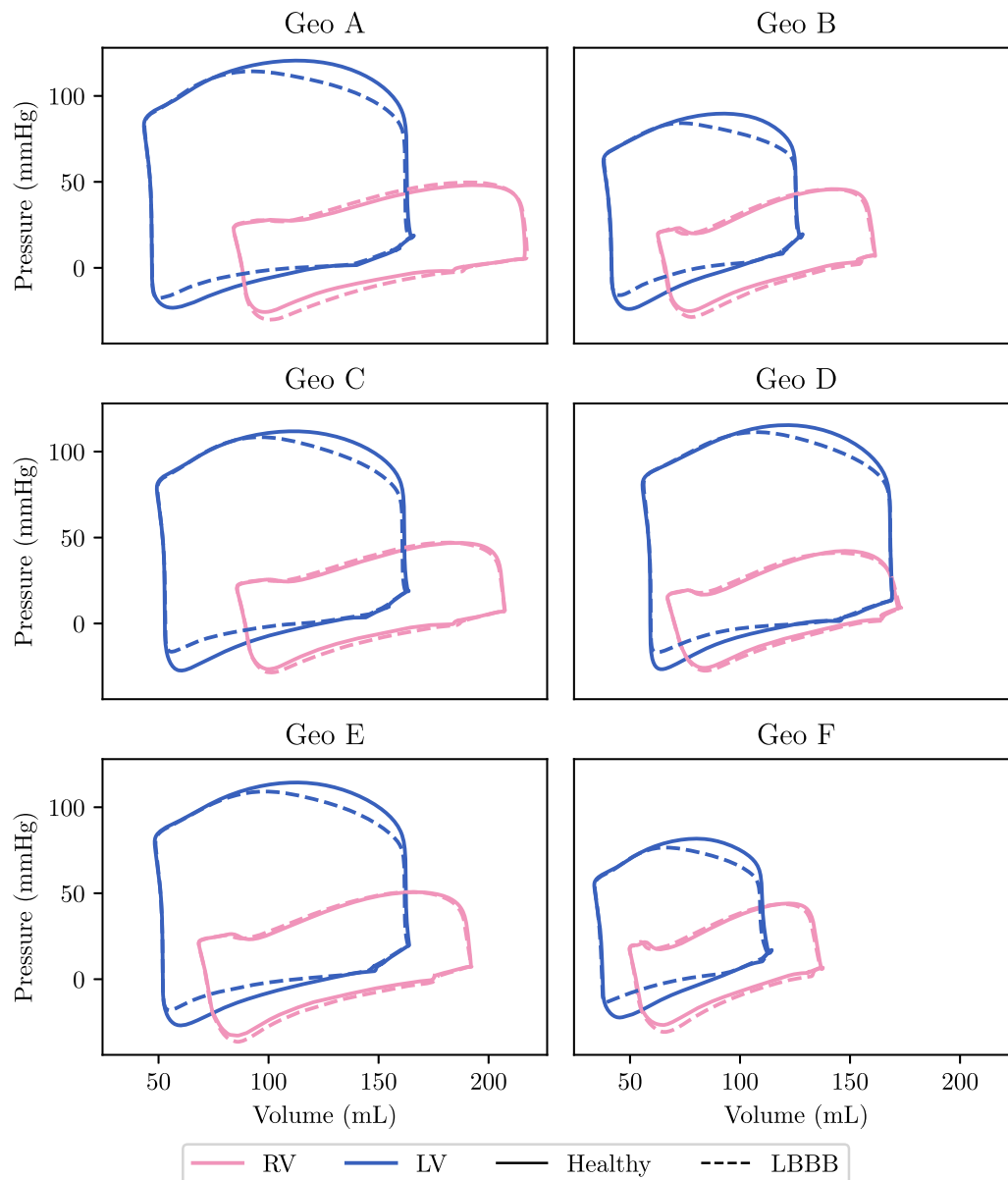


Figure 12. Comparison of pressure–volume loops (pV loops) between healthy and left bundle branch block (LBBB) cases for all geometries.

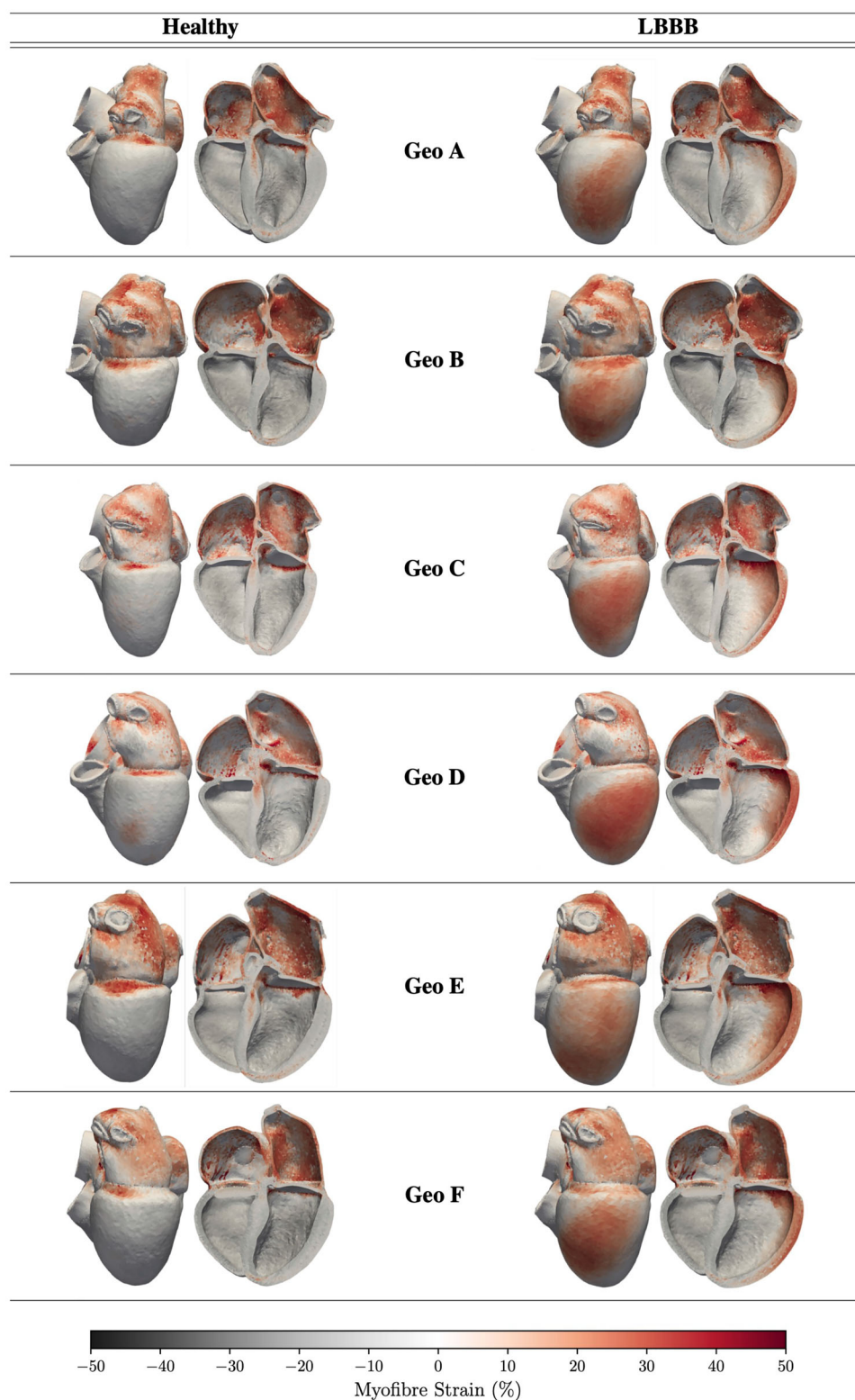


Figure 13. Myofibre strain in the whole heart at the beginning of ventricular contraction ($t = 360$ ms)
 The figure shows a comparison of the healthy and left bundle branch block (LBBB) case for each virtual patient. A prominent increase in LVfw strain and a thinning of the LVfw is visible for all LBBB cases.

employed a model incorporating full mechano-electric feedback. We would therefore expect our findings to remain valid if mechano-electric feedback were included in our model.

We incorporated variations in heart geometry, but the effects of different LBBB morphologies, including incomplete LBBB, were not considered.

Bramlet et al. (1983) observed patients with rate-dependent LBBB. They showed a decrease in LVEF from 62–6% after the onset of LBBB during exercise. Compared with our simulations this study demonstrates that electrical dyssynchrony in combination with an elevated heart rate can induce a stronger, but still non-pathological, reduction in pump function. Therefore, it would be interesting to see the impact that a higher heart rate would have on the *in silico* results. At a heart rate of 60 bpm, the duration of contraction remains sufficient to

allow complete ventricular contraction (Fig. 14), even in the presence of electromechanical dyssynchrony. Future studies could investigate the threshold heart rate at which full contraction is no longer feasible. However, such investigations are currently limited by the inability to model varying heart rates, as described in the work by Duhme et al. (2024).

In this study, we individualized the model parameterizations solely based on the patients' geometry. Apart from that, we did not consider a patient-specific parametrization due to data availability and conducted a sensitivity analysis only with respect to conduction velocity (Appendix A.9), which could be extended in future work. The complete LBBB scenario leads to a drastic delay in activation time in the LV, which is responsible for all acute changes emerging in mechanics and haemodynamics. Therefore, we do not expect any physiological amount of electrophysiological inter-patient variability, which would appear in both the healthy and LBBB scenarios, to be able to counter the strong impact of complete LBBB.

Regarding the impact of inter-patient variability on haemodynamics, left and right atrial preload exerted strong influence, while arterial and pulmonary arterial resistances exerted moderate influence, according to a global sensitivity analysis by Karabelas et al. (2022). Overall, their simulation results proved robust against inter-patient variability. This could also be explored in future work.

Conclusion

Our findings show that electrical and mechanical dyssynchrony do not immediately affect cardiac output. Mechanistic computational modelling allowed us to dissect isolated effects of pure and acute LBBB as a distinct contributor to the complex mechanisms underlying HF_d.

We observed acute electrical dyssynchrony causing mechanical dyssynchrony, manifesting as SF. The mechanical dyssynchrony was accompanied by a substantial strain increase in the LVfw but no immediate change in cardiac output. We hypothesize that the load imbalance between both ventricles, evidenced by the strain increase, drives adverse remodelling and impairs haemodynamics in the long run.

Underpinning clinical observations, our results provide a mechanistic basis for a likely benefit of an early pre-remodelling application of CRT in patients with LBBB. They also stress the importance of mechanical metrics to predict the long-term efficacy of pacing treatments.

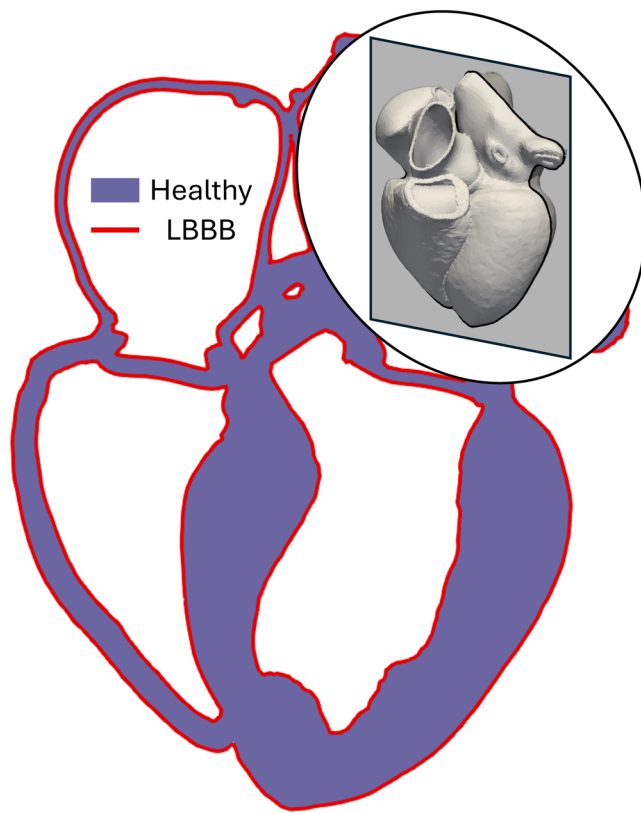


Figure 14. Sliced overlay of the healthy (blue surface) and left bundle branch block (LBBB) (red outline) simulations for geometry A at the time of full ventricular contraction ($t = 630$ ms)

The inset in the upper right corner shows the position of the slice in the deformed 3D heart geometry.

Appendix A

A.1 Patient-specific data

Table A1. Patient-specific data from Rodero et al. (2021b)

Paper ID	Rodero ID	Sex	Age (years)	Weight (kg)
A	04	M	39	92
B	07	F	50	95
C	08	M	47	NA
D	09	M	67	73
E	11	M	56	146
F	12	M	57	72

The utilized geometries were selected for their compatibility with the preprocessing workflow.

A.2 Ventricular regions

Table A2. Thresholds for the transmural coordinate (tm) used to capture transmural heterogeneity in the ventricles

Subepicardium	Mid-myocardium	Subendocardium
$tm \leq 0.2$	$0.2 < tm < 0.7$	$tm \geq 0.7$

According to the transmural coordinate the myocardium in the middle of the septum would be considered as sub-epicardium. We used the Laplace solution for the transventricular (tv) coordinate to identify this septal region and label it to be mid-myocardium.

A.3 Mechanical model parameters

Table A3. Active tension parameters for the whole-heart model. Adapted from Gerach, Schuler et al. (2023)

Parameter	Value		Unit	Description
	Atria	Ventricles		
$\lambda_{f,0}$	0.7	0.7	–	Minimum fibre stretch
t_{emd}	0.01	0.03	s	Electromechanical delay
T_{peak}	50 (RA), 80 (LA)	900 (RV), 450 (LV)	kPa	Peak isometric tension
t_{dur}	0.196	0.48	s	Duration of active contraction
τ_c	0.049	0.065	s	Time constant for relaxation
$\tau_{c,0}$	0.047	0.195	s	Time constant for active contraction
γ'	5.0	5.0	–	Degree of length dependency
γ'_{up}	0.5	0.5	s	Length dependency of upstroke time
t_{cycle}	1	1	s	Basic cycle length

Table A4. Mechanical model parameters in the myocardium adapted from Gerach & Loewe (2024)

Parameter	Value	Unit	Description
κ	650×10^3	Pa	Bulk modulus
C	880	Pa	Base material stiffness
b_{ff}	8	–	Fibre strain scaling
b_{ss}	6	–	Sheet strain scaling
b_{mn}	3	–	Cross-fibre in-plane strain scaling
b_{fs}	12	s	Shear strain in-plane scaling
b_{fn}	3	s	Shear strain in-plane scaling
b_{sn}	3	s	Shear strain in-plane scaling

Table A5. Mechanical model parameters in the valves, vessel trunks, orifices and pericardium adapted from Gerach & Loewe (2024)

Parameter	Value	Unit	Description
$\mu^{MV,TV,AV,PV}$	1×10^6	Pa	Shear modulus in the valves
$\kappa^{MV,TV,AV,PV}$	650×10^3	Pa	Bulk modulus in the valves
μ^{OR}	7.45×10^3	Pa	Shear modulus in the orifices
κ^{OR}	650×10^3	Pa	Bulk modulus in the orifices
$\mu^{ART,VEN}$	15.18×10^3	Pa	Shear modulus in the vessels
$\kappa^{ART,VEN}$	650×10^3	Pa	Bulk modulus in the vessels
μ^P	1×10^4	Pa	Shear modulus in the pericardium
κ^P	650×10^3	Pa	Bulk modulus in the pericardium
ρ_0	1082	kg ⁻³	Mass density in the entire mesh
$K_{\perp}$	1×10^7	Pa m ⁻¹	Contact penalty in normal direction on master and slave surface

Table A6. Geometry-specific mechanical parameters obtained by Klotz curve fitting

Geometry	Parameter	Value	Description
Geo	C_{scale}^{RA}	0.0420.084	Scaling for C in the RA
A,	C_{scale}^{LA}	0.07	Scaling for C in the LA
B,	$C_{scale}^{RV,LV}$	3.55	Scaling for C in the RV and LV
Geo	b_{scale}	3.363	Scaling for b_{xx}
C	C_{scale}^{RA}	0.1120.134	Scaling for C in the RA
	C_{scale}^{LA}	0.067	Scaling for C in the LA
	$C_{scale}^{RV,LV}$	3.363	Scaling for C in the RV and LV
Geo	b_{scale}	0.1530.184	Scaling for b_{xx}
D	C_{scale}^{RA}	0.092	Scaling for C in the RA
	C_{scale}^{LA}	2.949	Scaling for C in the LA
	$C_{scale}^{RV,LV}$	0.1040.125	Scaling for C in the RV and LV
Geo	b_{scale}	0.063	Scaling for b_{xx}
E	C_{scale}^{RA}	3.165	Scaling for C in the RA
	C_{scale}^{LA}		Scaling for C in the LA
	$C_{scale}^{RV,LV}$		Scaling for C in the RV and LV
	b_{scale}		Scaling for b_{xx}

A.4 Additional mechanical measurements

Table A7. Maximum myofibre strain in % for all geometries

Geometry		LVfw
	Healthy	LBBB
A	14.02	18.23
B	18.31	20.56
C	17.5	20.51
D	18.29	22.2
E	18.38	21.75
F	18.65	21.17

A.5 Pseudo M-mode images for geometries B–F

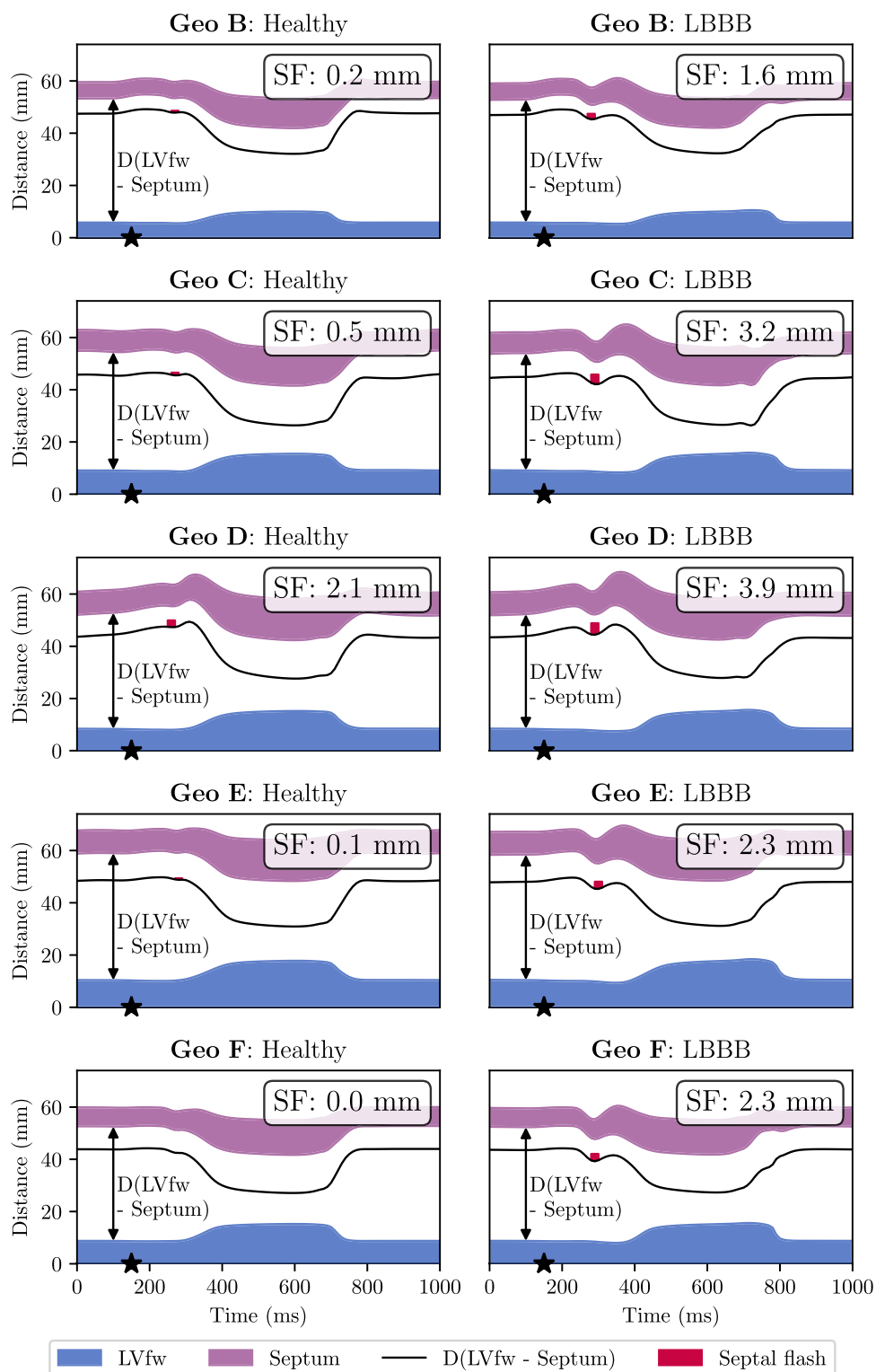


Figure A1. Pseudo M-mode for geometries B, C, D, E and F

This comparison visualizes the variance in wall thickness and chamber size between the geometries. The activation of the atrioventricular node is marked with a black star.

A.6 Additional haemodynamic measurements

Table A8. Ejection fraction (EF) in % for all geometries

Geometry	RV		LV	
	Healthy	LBBB	Healthy	LBBB
A	62.63	62.71	73.89	73.7
B	61.94	62.01	70.51	70.29
C	59.5	59.55	69.94	69.69
D	61.09	61.38	68.08	67.8
E	64.92	65.02	70.57	70.28
F	64.31	64.32	70.52	70.32

Table A9. Stroke volume in mL for all geometries

Geometry	RV		LV	
	Healthy	LBBB	Healthy	LBBB
A	139.89	140.07	122.71	122.13
B	101.17	101.27	90.58	90.23
C	125.05	125.15	114.51	113.77
D	105.19	106.37	118.73	118.24
E	125.79	126.22	115.7	114.93
F	89.17	89.18	80.71	80.34

Table A10. Maximum rate of systolic pressure rise (dp/dtmax) in mmHg/s for all geometries

Geometry	RV		LV	
	Healthy	LBBB	Healthy	LBBB
A	0.94	0.86	1.98	1.35
B	0.98	0.92	1.48	0.97
C	0.91	0.79	1.59	1.03
D	0.76	0.68	1.48	1.2
E	0.99	1.0	1.67	1.11
F	1.01	0.9	1.46	0.88

Table A11. Maximum pressure in mmHg for all geometries

Geometry	RV		LV	
	Healthy	LBBB	Healthy	LBBB
A	48.12	49.71	120.55	114.31
B	45.76	45.8	89.71	84.2
C	46.95	47.14	111.83	108.41
D	42.23	41.08	115.4	111.32
E	50.65	50.75	114.41	109.15
F	44.07	43.68	81.73	76.59

A.7 Interpretation septal flash geometry D

In the M-mode plots (Fig. 8, Fig. A1), septal flashes (SF) associated with left bundle branch block (LBBB) are consistently characterized by a septal movement toward the left ventricular free wall (LVfw), whereas the healthy simulation in geometry D exhibits a prominent septal motion toward the right ventricular free wall (RVfw).

Geometry D has an unusually small right ventricle (RV) with a nearly concave lateral wall. Out of all six geometries, only geometry D exhibited comparable right ventricle (RV) and left ventricle (LV) end diastolic volumes (EDVs), whereas the RV EDV exceeded the LV EDV in all other cases (Fig. 12). In the healthy case, the LV peak pressure reaches 2.73 times that of the RV – the highest ratio among all geometries. Additionally, pressure rise in both chambers occurs almost simultaneously (Fig. A2). This synchronous pressure development is also observed in geometries B and F, though at lower pressures and reduced LV/RV peak pressure ratios of 1.96 and 1.85, respectively.

Collectively, these observations suggest that the pronounced SF in the healthy simulation of geometry D arises from the LV's elevated pressure overcoming the RV pressure during early contraction, which pushes the septum toward the RVfw. This pressure–contraction imbalance is a direct consequence of the patient-specific geometry, where a comparatively underdeveloped RV is paired with a structurally dominant LV.

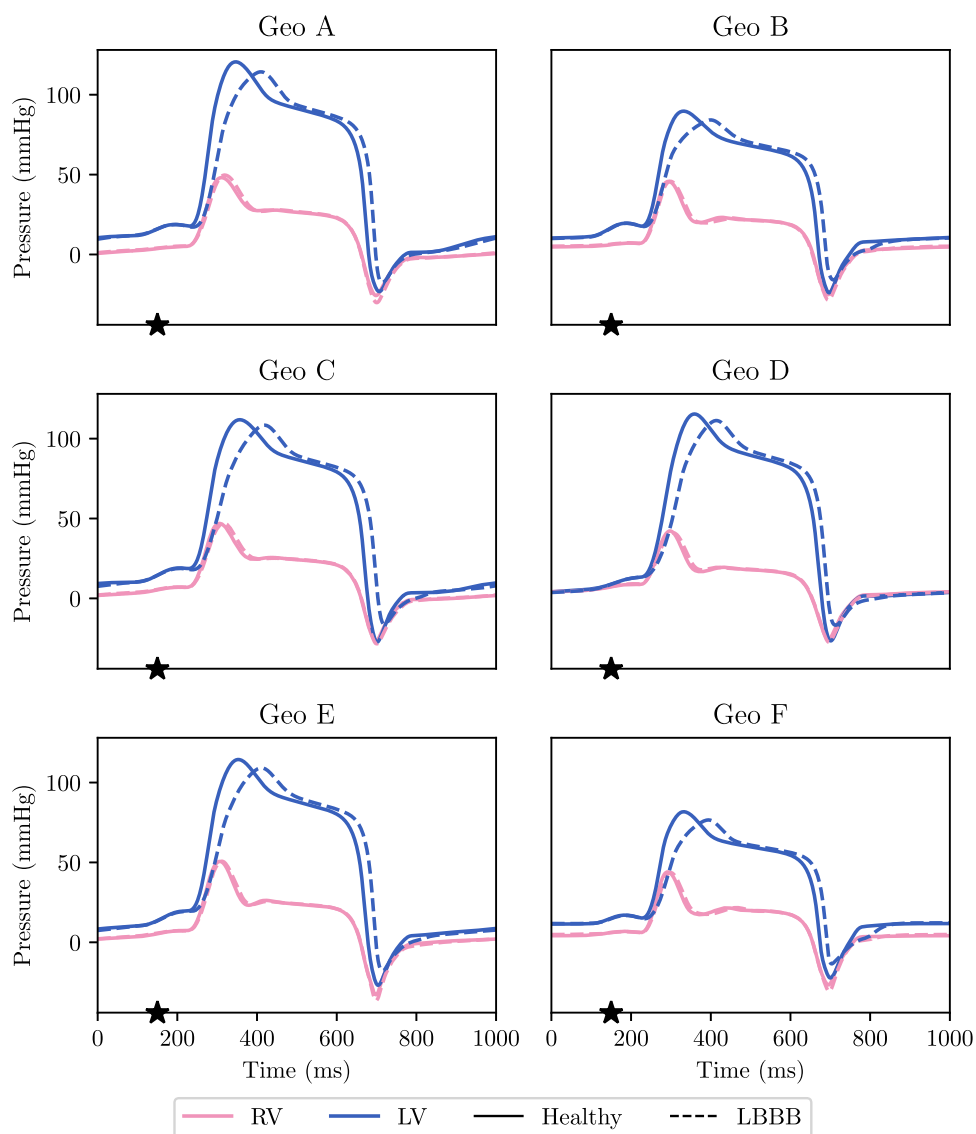


Figure A2. Comparison of ventricular pressure over time between healthy and left bundle branch block cases for all geometries

The activation of the atrioventricular node is marked with a black star.

A.8 The effect of the Frank-Starling mechanism in ejection fraction preservation

Considering the sizeable increase in LVfw strain for LBBB, increased force-generation due to the Frank-Starling mechanism might assist in the preservation of LVEF. In the tension model by Niederer et al. (2011) the effect of the Frank-Starling mechanism is modelled by the original length dependence of the tension model (γ). To test the role Frank-Starling mechanism plays in LVEF preservation, we ran simulations with half the original γ for both cases across all geometries. Under this modified length dependence, relative EF changes for the healthy cases vs the LBBB cases were more than twice as large compared with the original simulations (Fig. A3). These results support the hypothesis that a strong Frank-Starling mechanism can facilitate EF preservation. However, even in the altered simulations the changes in EF stay under 2%. We therefore consider the upkeep of full ventricular contraction as seen in Fig. 14 to be the main mechanism in EF preservation for our simulation scenario.

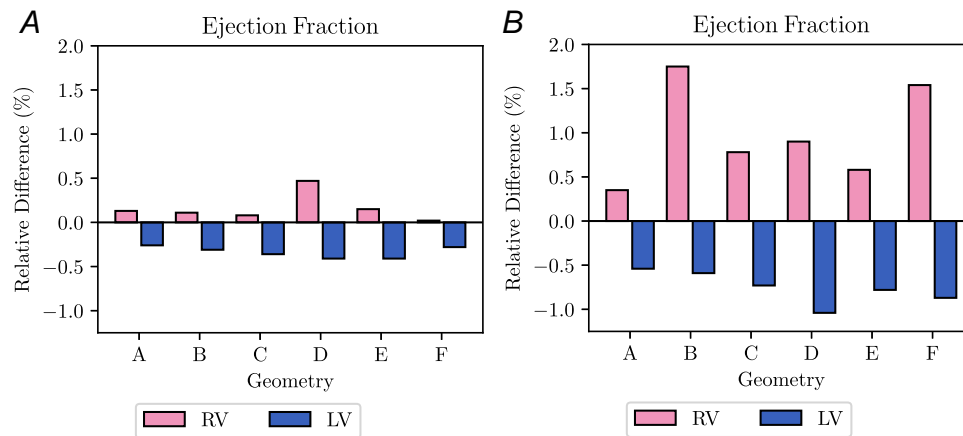


Figure A3. Relative difference in ejection fraction between healthy and left bundle branch block cases for all geometries

A: Original degree of length dependence of the tension model ($\gamma = 5$). B: Reduced degree of length dependence of the tension model ($\gamma = 2.5$). The relative difference for ejection fraction (EF) is calculated as follows: $(EF(LBBB) - EF(Healthy))/EF(Healthy)$.

A.9 Sensitivity analysis for conduction velocities

To assess sensitivity to conduction velocity, we performed two additional simulations for geometry A, scaling ventricular conduction velocity by factors of 0.8 and 1.2. Results are shown in Table A12, Table A13 and Fig. A4. With both slowed ($0.8 \times$ original CV) and increased ($1.2 \times$ original CV) conduction velocity, delayed left ventricular activation following LBBB remained pronounced.

Complete LBBB causes a drastic change in activation times. This effect is far larger than physiological inter-patient variability in conduction velocity, which would occur in both the healthy and LBBB scenarios. We therefore expect our findings to be robust to such inter-patient variability.

Table A12. Ventricular uncoupling (VEU) of both ventricles for the simulation with original conduction velocities (CVs) compared with the ones with scaled CVs (0.8, 1.2)

	Healthy			LBBB		
	0.8	1	1.2	0.8	1	1.2
CV scaling						
VEU (ms)	4.44	3.73	3.24	44.53	39.42	35.75

Table A13. Total activation times (TAT) of both ventricles of geometry A. Comparison between the simulations with original conduction velocities (CVs) compared with the ones with scaled CVs (0.8, 1.2)

	Healthy			LBBB		
	0.8	1	1.2	0.8	1	1.2
CV scaling						
TAT (ms)	97.68	88.74	82.43	154.02	139.3	128.73

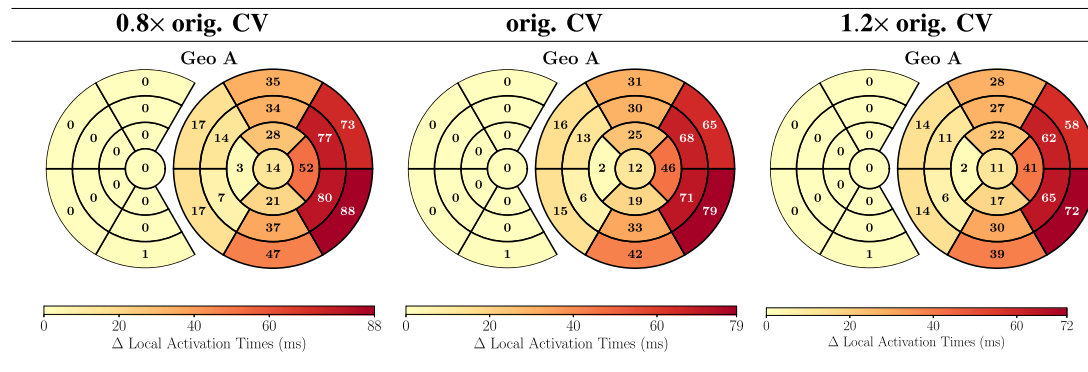


Figure A4. Bullseye plots of absolute difference in local activation times between healthy and left bundle branch block case for geometry A
Comparison between the simulations with original conduction velocities (CVs) and scaled CVs (0.8, 1.2).

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Additional information

Data availability statement

The original geometries from the Rodero et al. (2021a) cohort are available under the Creative Commons Attribution 4.0 International license. The original contributions presented in the study are included in the article. The simulation software (openCARP (openCARP consortium et al., 2026) and Cardio-Mechanics (Gerach, Fritz et al., 2023)) is openly available. The complete simulation setups are available on <https://doi.org/10.5281/zenodo.21934381>

Competing interests

All authors declare that they have no conflict of interest.

Author contributions

C.K.: Conceptualization, Methodology, Investigation, Analysis, Writing – Original Draft, Visualization. J.K.: Conceptualization, Methodology, Analysis, Writing – Review & Editing, Supervision. J.S.: Methodology, Software, Writing – Review & Editing. T.G.: Methodology, Software, Writing – Review & Editing. C.B.E.: Conceptualization, Writing – Review & Editing. J.E.D.: Software, Writing – Review & Editing. A.L.: Conceptualization, Analysis, Writing – Review & Editing, Supervision, Funding acquisition. All authors approved the final version of the manuscript.

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The generative AI model Le Chat (Mistral AI) was utilized for coding plotting scripts and assisting in the preparation of this manuscript. After using this service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Keywords

cardiac digital twin, cardiac resynchronization therapy, computational modelling, electromechanical modelling, left bundle branch block

Supporting information

Additional supporting information can be found online in the Supporting Information section at the end of the HTML view of the article. Supporting information files available:

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