Prediction of Response to Cardiac Resynchronization Therapy (CRT) using *In Silico* Heart Model: Pilot Study of Comparison between *In Silico* & Real CRT Outcomes

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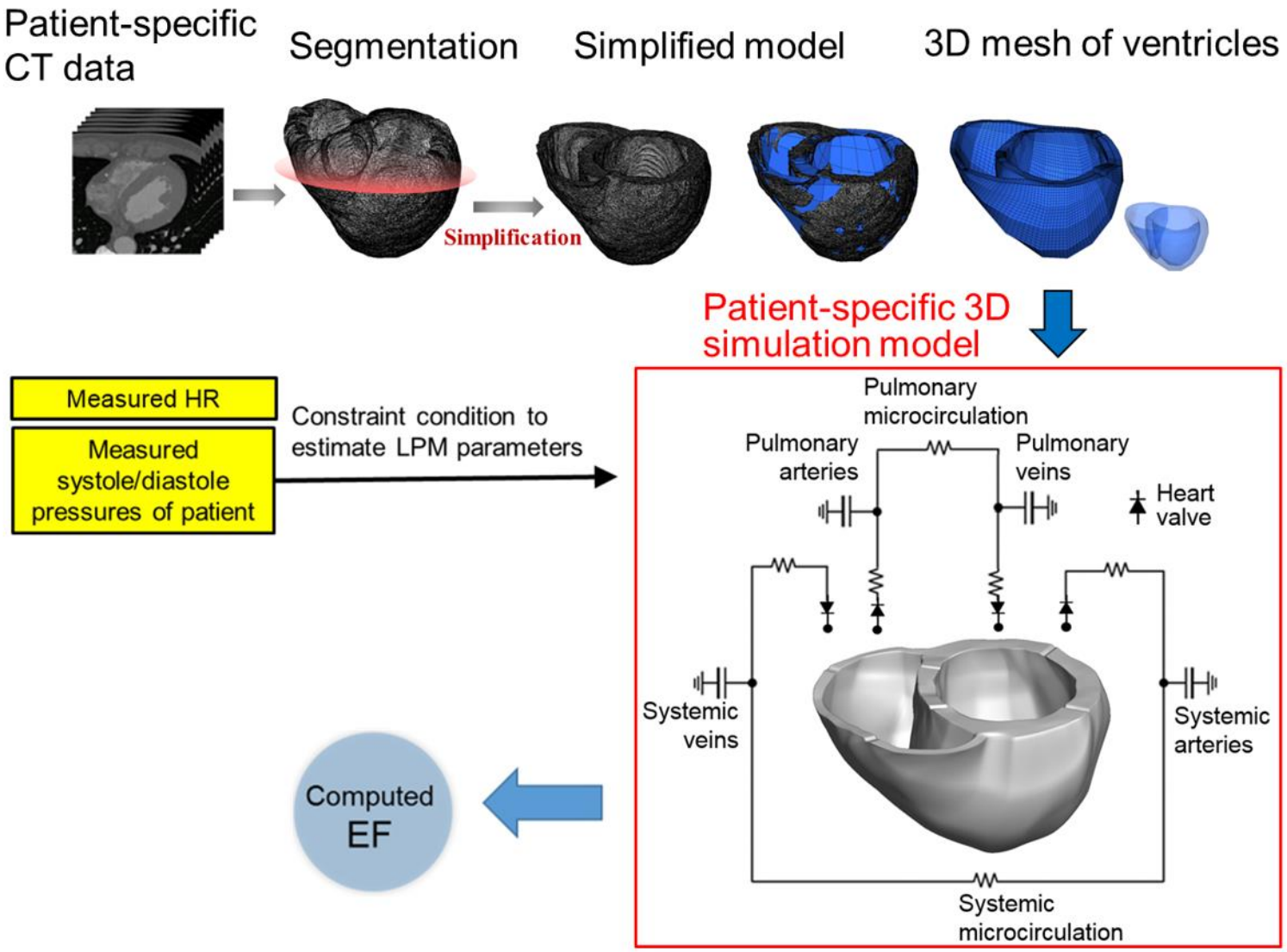
Introduction

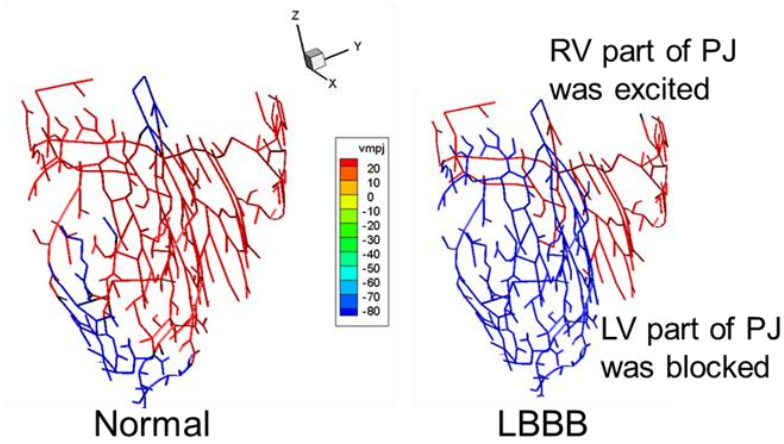
- Cardiac resynchronization therapy (CRT) is an effective treatment in patients with heart failure with reduced ejection fraction (EF) and left bundle branch block.
- However, about 1/3 of the patients with CRT are non-responders to CRT.
- If CRT response can be predicted, we can avoid implanting CRT for non-responder-to-be.
- We recently developed the *in silico* CRT modeling for prediction of CRT response.
- The objective of this study was to validate the accuracy of the *in silico* model.

Methods: *In Silico* Heart Model

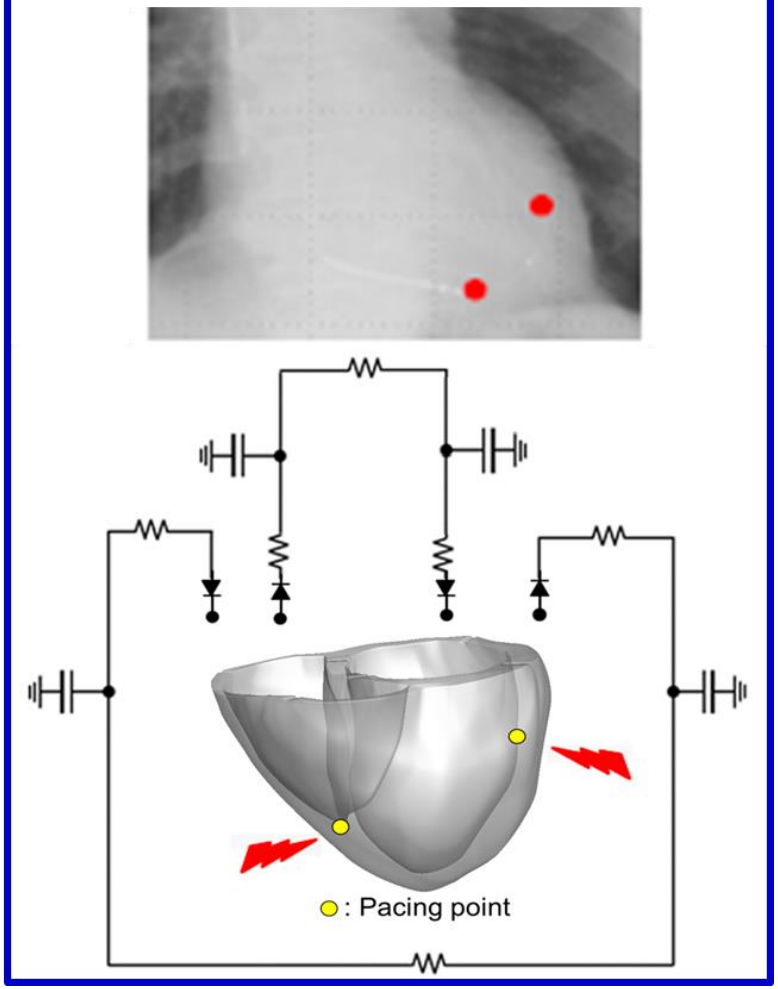


Methods: CRT Simulation Model

LBBB simulation model



CRT simulation model



Methods: CRT Simulation Model

Clinical data of the patient

- Left bundle branch block (LBBB), left ventricular end-diastolic/systolic volume (LVED/SV), EF
- Systole/Diastole Blood Pressure (BP), Heart rate(HR)

↓

Construction of the patient-specific 3D ventricular model

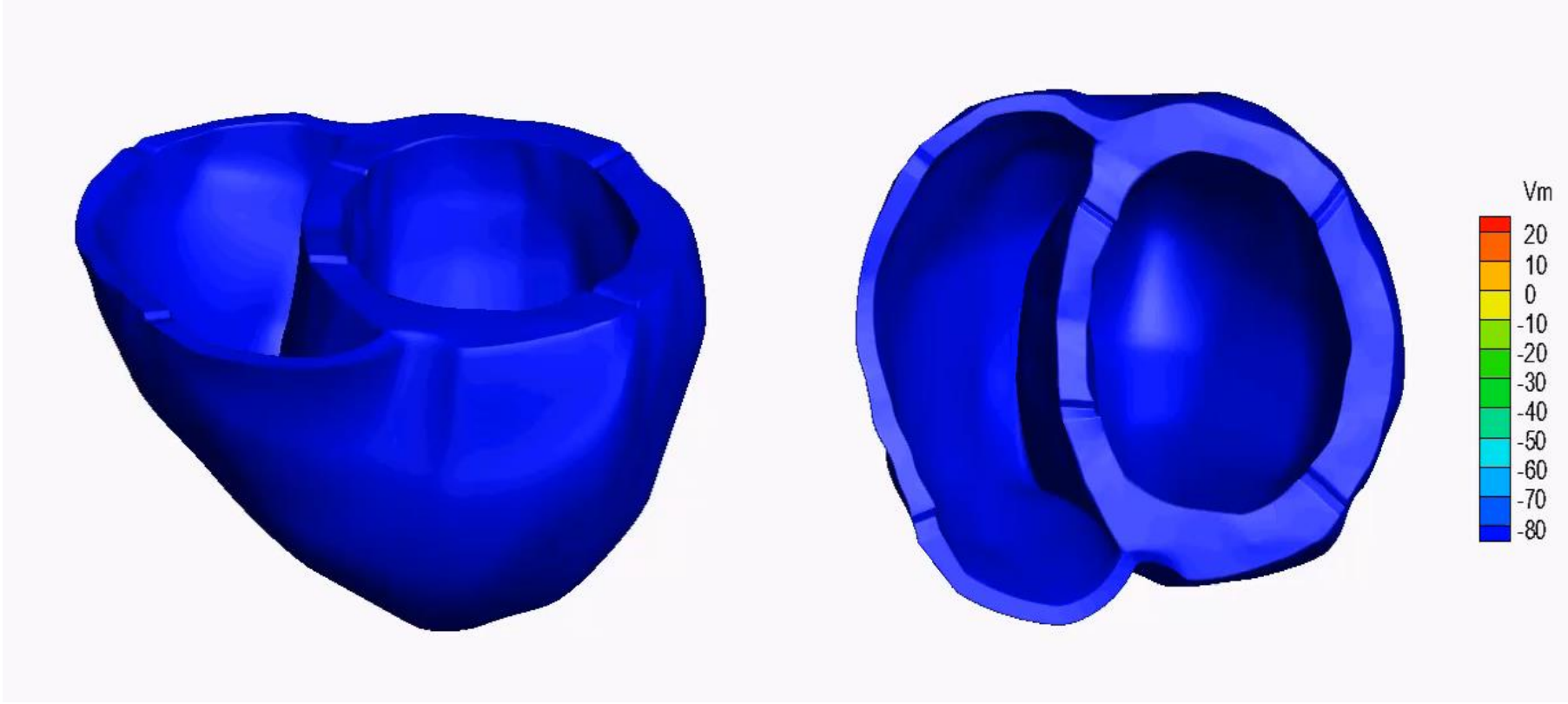
- Extraction of the 3D geometry from CT image segmentation
- Addition of Purkinje fibers to the 3D geometric model

↓

Main simulation procedure

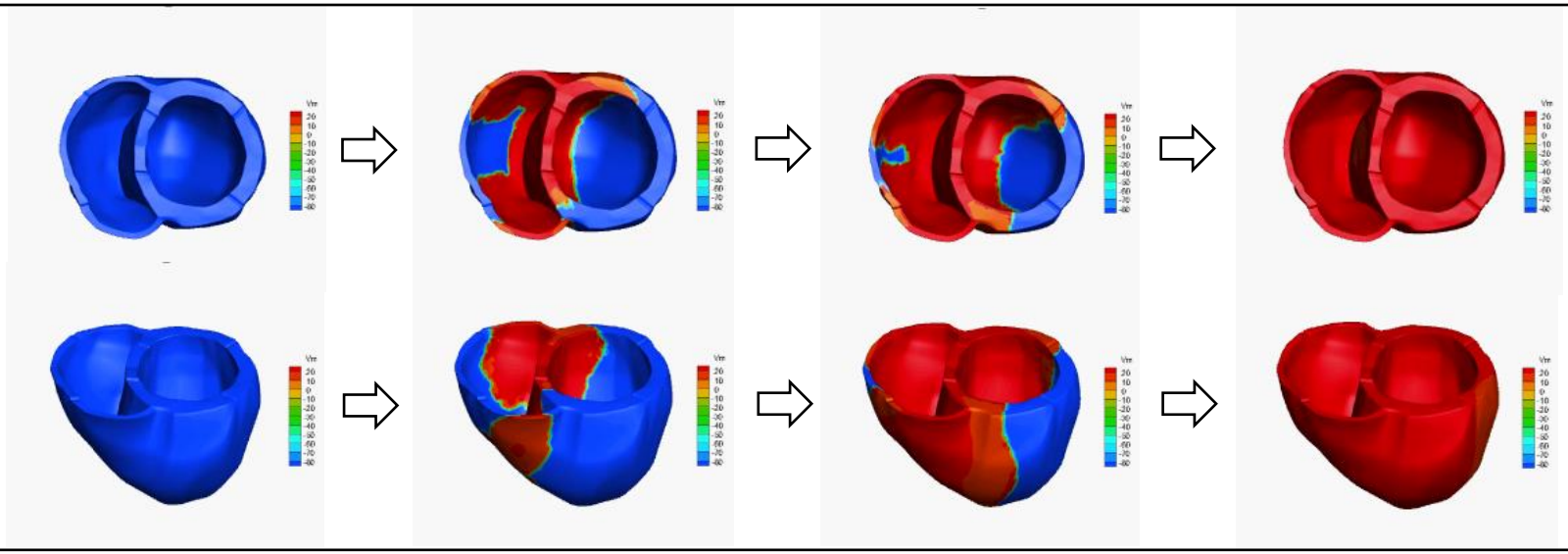
- Step 1 : Assuming the resistance (R) and capacitance (C) values of the vascular system
- Step 2 : Coupling the resistances and capacitances with the 3D ventricular model
- Step 3 : Simulation of the coupled model → Computation of sys/dias BP and EF
- Step 4 : Comparison of the computed sys/dias BP and EF with the clinical data
- Step 5 : Assume new R and C values and go to step 2 if the errors > 5 %
  Go to step 6 if the errors < 5 % (the assumed R & C → the patient-specific values)
- Step 6 : Computation of the CRT simulation model by pacing the heart
- Step 7 : Determination of responder or non-responder by the computed EF

Methods: Example of *In Silico* Heart Model

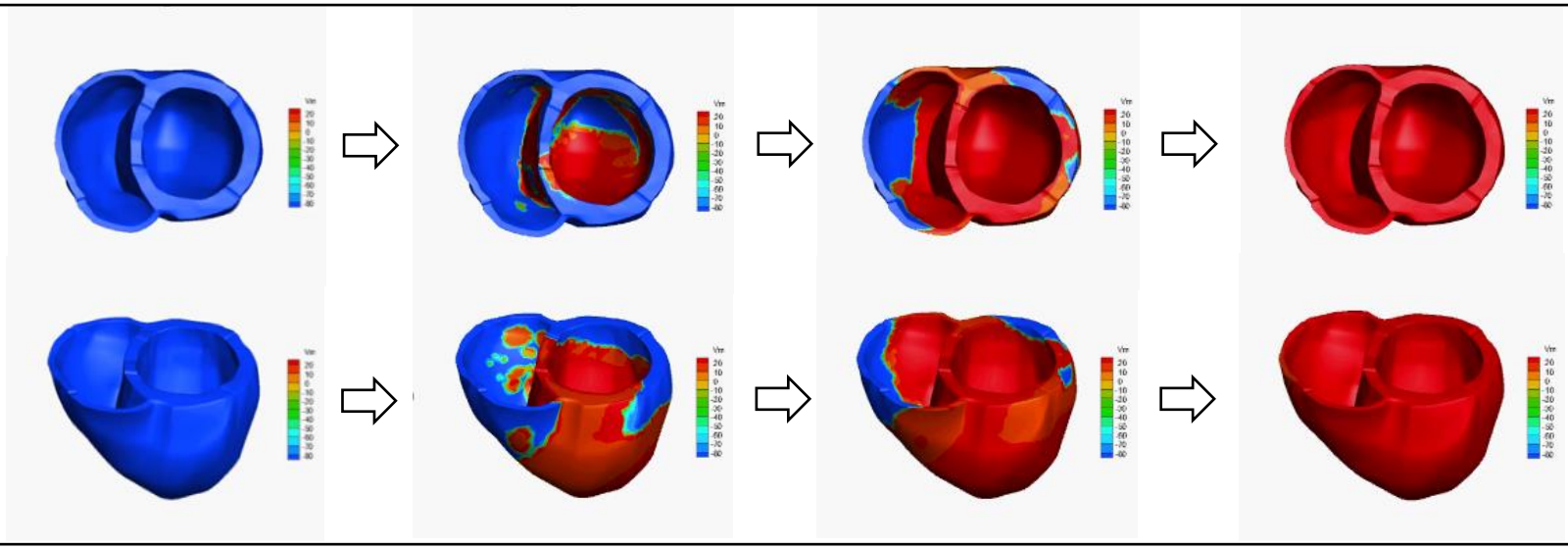


Methods: CRT Simulation Model

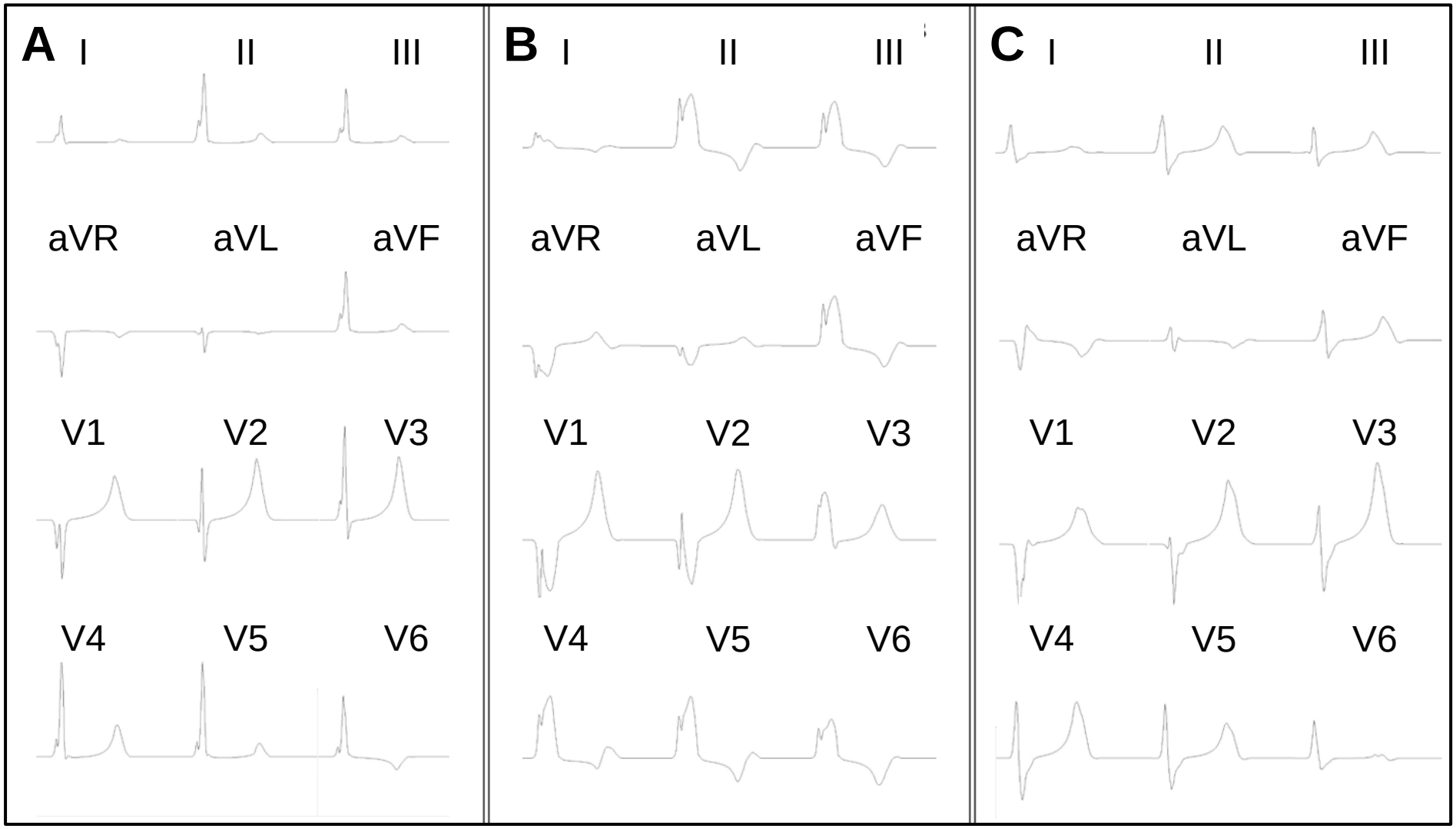
LBBB



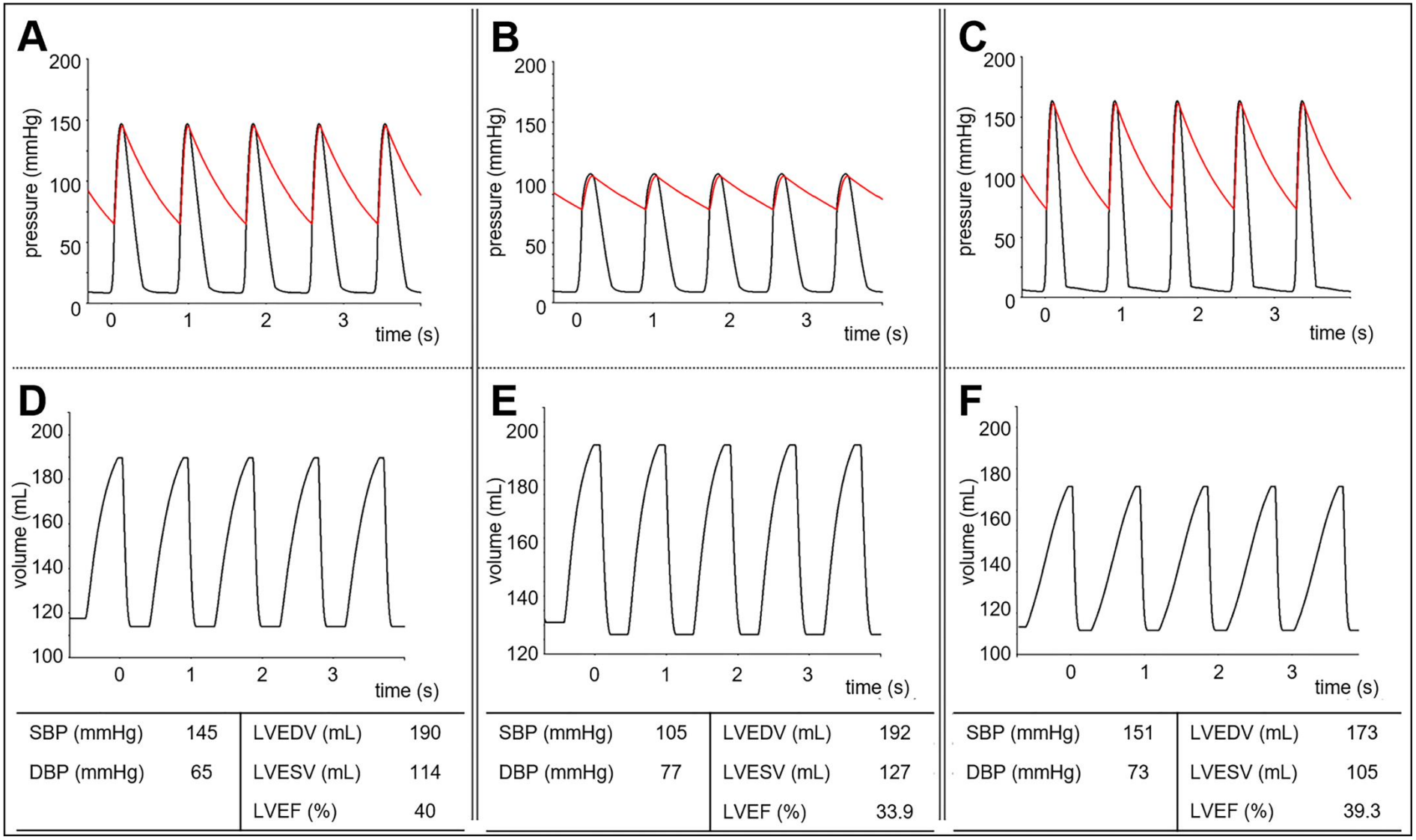
CRT



ECG Simulation



Results: *In Silico* CRT Simulation



SBP (mmHg)	145	LVEDV (mL)	190
DBP (mmHg)	65	LVESV (mL)	114
		LVEF (%)	40

SBP (mmHg)	105	LVEDV (mL)	192
DBP (mmHg)	77	LVESV (mL)	127
		LVEF (%)	33.9

SBP (mmHg)	151	LVEDV (mL)	173
DBP (mmHg)	73	LVESV (mL)	105
		LVEF (%)	39.3

Methods

- We retrospectively included 11 patients (age, 64.0 ± 11.2 years, 4 men) with CRT who underwent cardiac computed tomography (CT) and magnetic resonance (MR) before CRT implantation.
- To construct the *in silico* CRT model, we combined the 3D image using cardiac CT and MR images, based on electromechanical ventricular model with a lumped model of the circulatory system and electric pacing device.

Methods

- *In silico* CRT responder was defined as absolute increase in LVEF ≥ 5%
- We retrospectively compared *in silico* CRT response with real CRT response.

Results

			In silico			Real			
Age	Sex	HF cause	$LVEF_{pre\text{-}CRT}$ (%)	$LVEF_{post\text{-}CRT}$ (%)	Response	$LVEF_{pre\text{-}CRT}$ (%)	$LVEF_{post\text{-}CRT}$ (%)	Response	Agreement
58	F	Non-ischemic	32.2	29.6	No	17.1	20.1	No	Yes
70	F	Non-ischemic	33.8	37.0	Yes	14.3	32.3	Yes	Yes
66	F	Non-ischemic	16.4	17.2	No	27.1	43.5	Yes	No
78	F	Non-ischemic	20.6	21.3	No	18.7	19.3	No	Yes
60	F	Non-ischemic	36.5	40.8	No	22.2	23.3	No	Yes
67	F	Ischemic	24.8	25.8	No	14.4	18.5	No	Yes
68	M	Non-ischemic	28.1	29.0	No	15.1	12.5	No	Yes
38	M	Non-ischemic	13.9	14.9	No	18.8	19.1	No	Yes
65	F	Non-ischemic	38.0	39.8	No	24.7	28.0	No	Yes
56	M	Non-ischemic	18.7	19.0	No	17.3	15.7	No	Yes
78	M	Non-ischemic	28.6	36.1	Yes	25.8	54.8	Yes	Yes

Results

- Two patients were *in silico* CRT responders, and those 2 patients were also real CRT responders.
- Nine patients were *in silico* CRT non-responders, 8 who were real CRT non-responders, and 1 who was a real CRT responder.
- The *in silico* CRT outcomes agreed with the real CRT outcomes in 10 of 11 patients.
- The positive and negative predictive values and accuracy of the *in silico* CRT model were 100%, 88.9%, and 90.9%, respectively.

Study Limitations

- This study was retrospective and used only a small number of patients. Large-scale prospective studies are needed to validate the accuracy of our *in silico* CRT simulation model.
- This *in silico* CRT simulation model was applied to the patients with only LBBB in this study. This *in silico* CRT simulation model need to be studied in patients with right bundle branch block or intraventricular conduction delay.

Conclusion

- The present *in-silico* CRT modeling is feasible for predicting real CRT outcomes.

Thank you

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