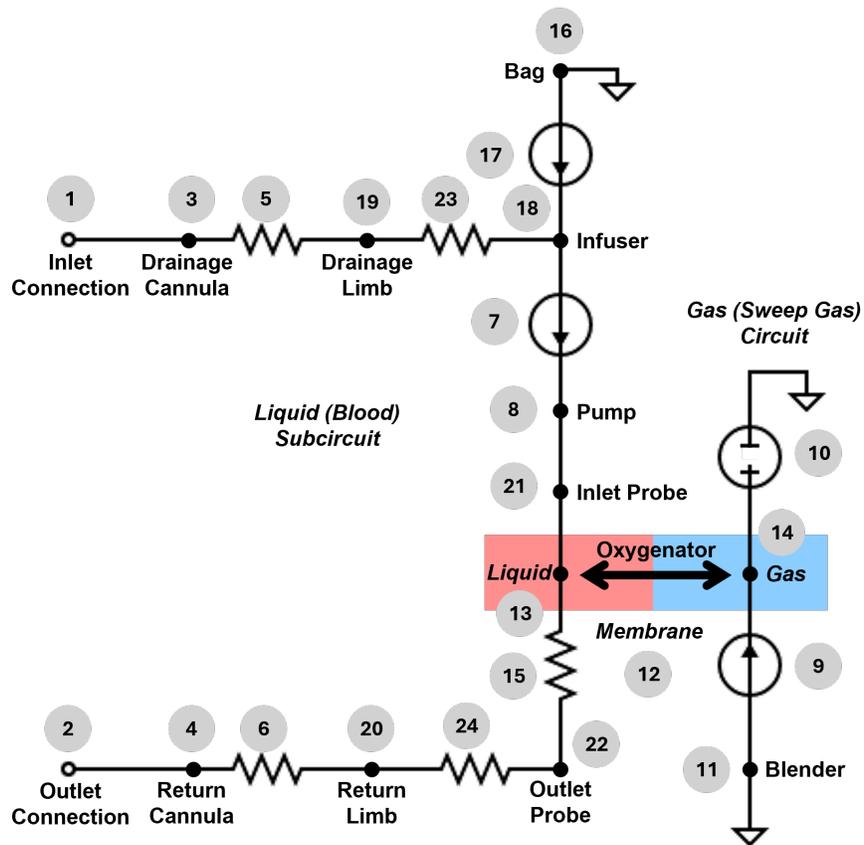# Supplementary Information

Supplementary Figure S1. Pulse Physiology Engine extracorporeal membrane oxygenation (ECMO) circuit configuration used in the digital twin simulations.

Supplementary Table S1. ECMO circuit parameters represented in the Pulse digital twin model.

Label	Parameter	Component
1	Inlet Location	
2	Outlet Location	
3	Drainage Cannula Volume	Cannulas
4	Return Cannula Volume	
5	Drainage Cannula Resistance	
6	Return Cannula Resistance	
7	Pump Flow	Pump
8	Pump Volume	
9	Sweep Gas Flow	
10	Supply Pressure	
11	Fraction of Sweep Gas Oxygen	
12	Oxygen Membrane Diffusing Capacity	
12	Carbon Dioxide Membrane Diffusing Capacity	Oxygenator
13	Oxygenator Liquid Volume	
14	Oxygenator Gas Volume	
15	Oxygenator Resistance	
16	Bag Compound	
16	Bag Volume	Fluid Administration
17	Infuser Rate	
18	Infuser Volume	
19	Drainage Limb Volume	
20	Return Limb Volume	
21	Inlet Probe Volume	Peripherals
21	Outlet Probe Volume	
23	Drainage Limb Resistance	
24	Return Limb Resistance	

Supplementary Table S2. Mechanical ventilator settings used to initialize patient digital twins, showing prescribed target values (Tgt) and resulting simulated values (Sim). Parameters include tidal volume (VT), respiratory rate (RR), positive end-expiratory pressure (PEEP), fraction of inspired oxygen (FiO$_2$), and plateau pressure (P$_{plat}$)

Patient	VT (mL)		RR (breaths/min)		PEEP (cmH$_2$O)		FiO$_2$ (%)		P$_{plat}$ (cmH$_2$O)	
	Tgt	Sim	Tgt	Sim	Tgt	Sim	Tgt	Sim	Tgt	Sim
P1	100.0	101.8	20.0	20.0	8.0	8.0	50.0	50.0	20.0	20.7
P2	200.0	197.3	30.0	29.7	6.0	6.0	50.0	50.0	21.0	21.8
P3	100.0	101.3	30.0	29.7	12.0	12.0	40.0	40.0	26.0	26.7
P4	100.0	101.3	30.0	29.7	8.0	8.0	40.0	40.0	22.0	22.7
P5	140.0	139.7	30.0	29.7	10.0	10.0	50.0	50.0	26.0	26.7
P6	100.0	101.3	30.0	29.7	10.0	10.0	40.0	40.0	25.0	25.7
P7	100.0	101.3	30.0	29.7	8.0	8.0	40.0	40.0	19.0	19.7
P8	120.0	120.5	30.0	29.7	5.0	5.0	40.0	40.0	20.0	20.7
P9	150.0	149.3	30.0	29.7	12.0	12.0	40.0	40.0	21.0	21.7
P10	120.0	120.5	30.0	29.7	10.0	10.0	40.0	40.0	22.0	22.7

Supplementary Table S3. Venovenous ECMO (VV-ECMO) circuit settings prescribed for patient digital twin simulations, showing target (Tgt) and simulated (Sim) values for ECMO blood flow, sweep gas flow, and sweep gas oxygen fraction.
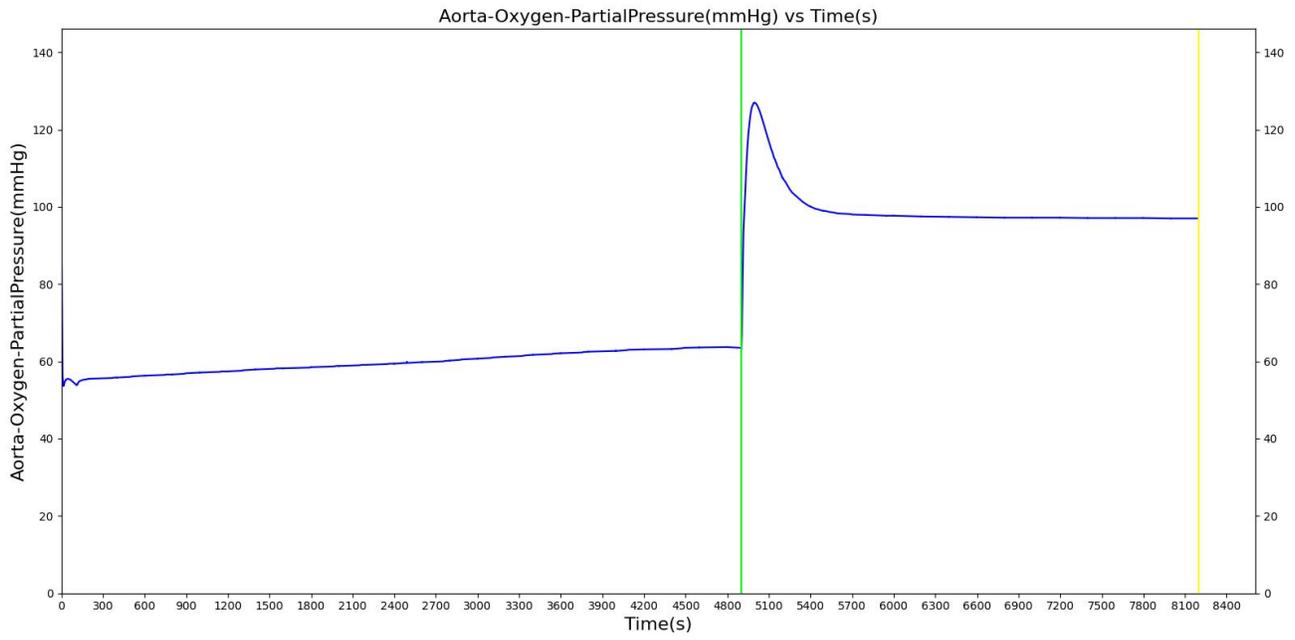
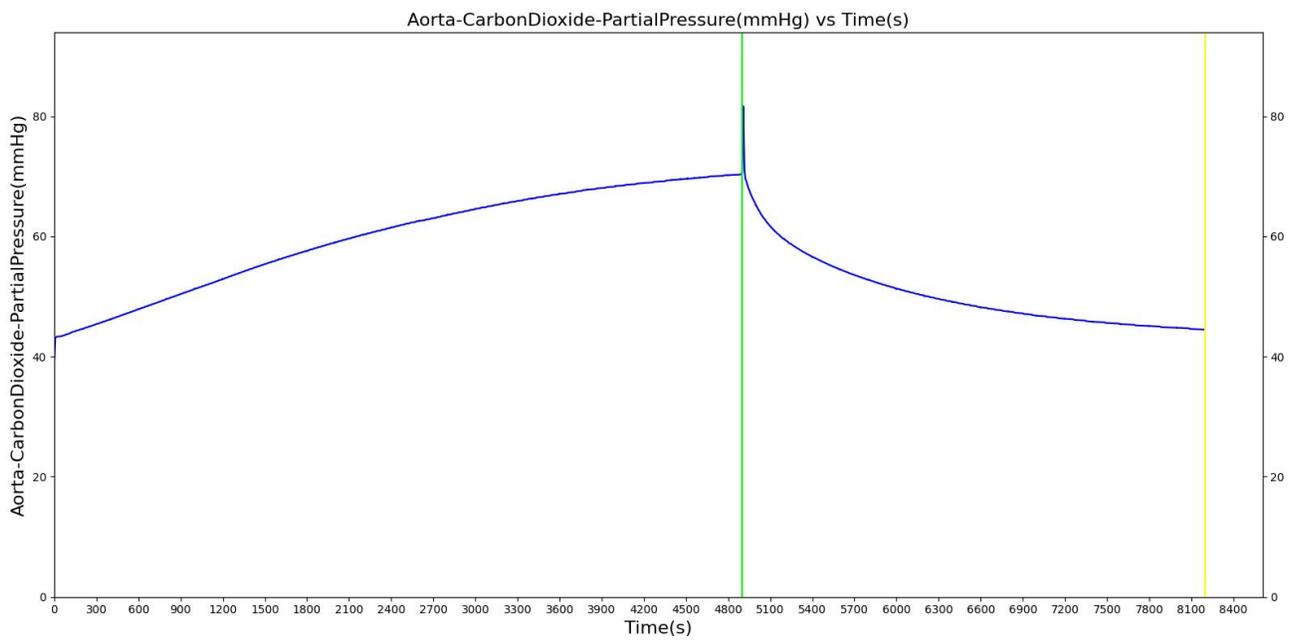| Patient	ECMO Blood Flow (L/min)		Sweep Gas Flow (L/min)		Sweep Gas Oxygen Fraction (%)	
	Tgt	Sim	Tgt	Sim	Tgt	Sim
P1	6.8	6.8	6.0	6.0	100.0	100.0
P2	5.6	5.6	6.0	6.0	100.0	100.0
P3	5.3	5.3	6.0	6.0	100.0	100.0
P4	4.5	4.5	6.0	6.0	100.0	100.0
P5	5.6	5.6	6.0	6.0	100.0	100.0
P6	5.3	5.3	6.0	6.0	100.0	100.0
P7	6.9	6.9	6.0	6.0	100.0	100.0
P8	6.8	6.8	6.0	6.0	100.0	100.0
P9	6.0	6.0	6.0	6.0	100.0	100.0
P10	5.0	5.0	6.0	6.0	100.0	100.0
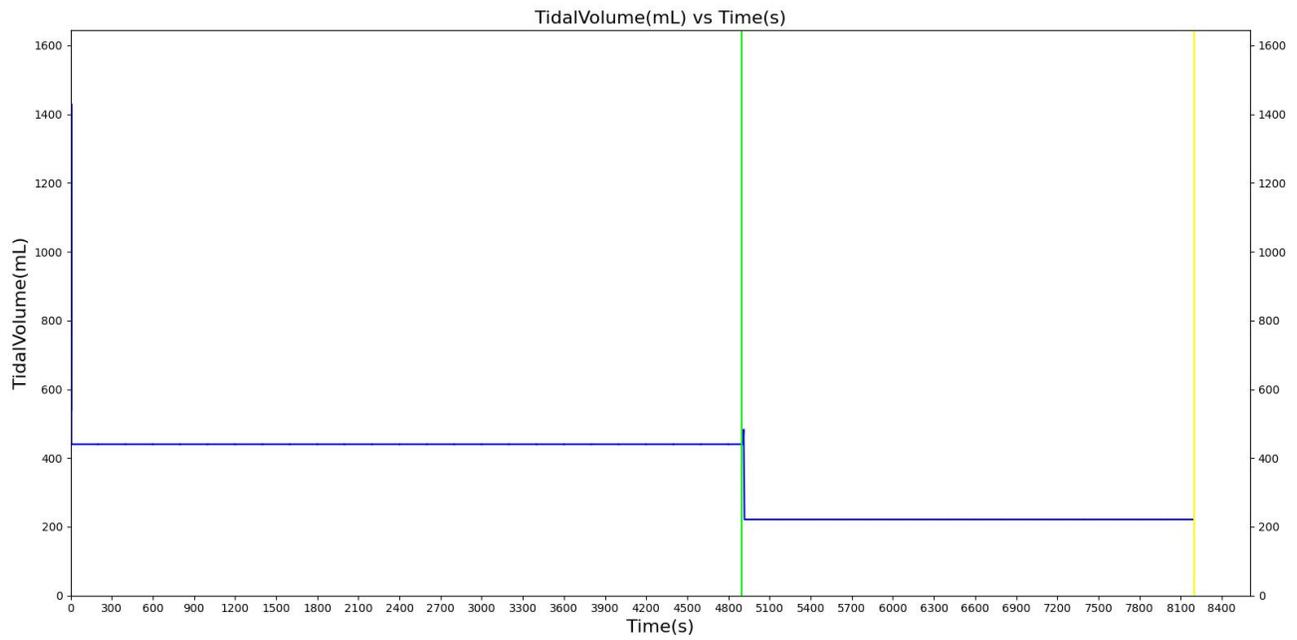
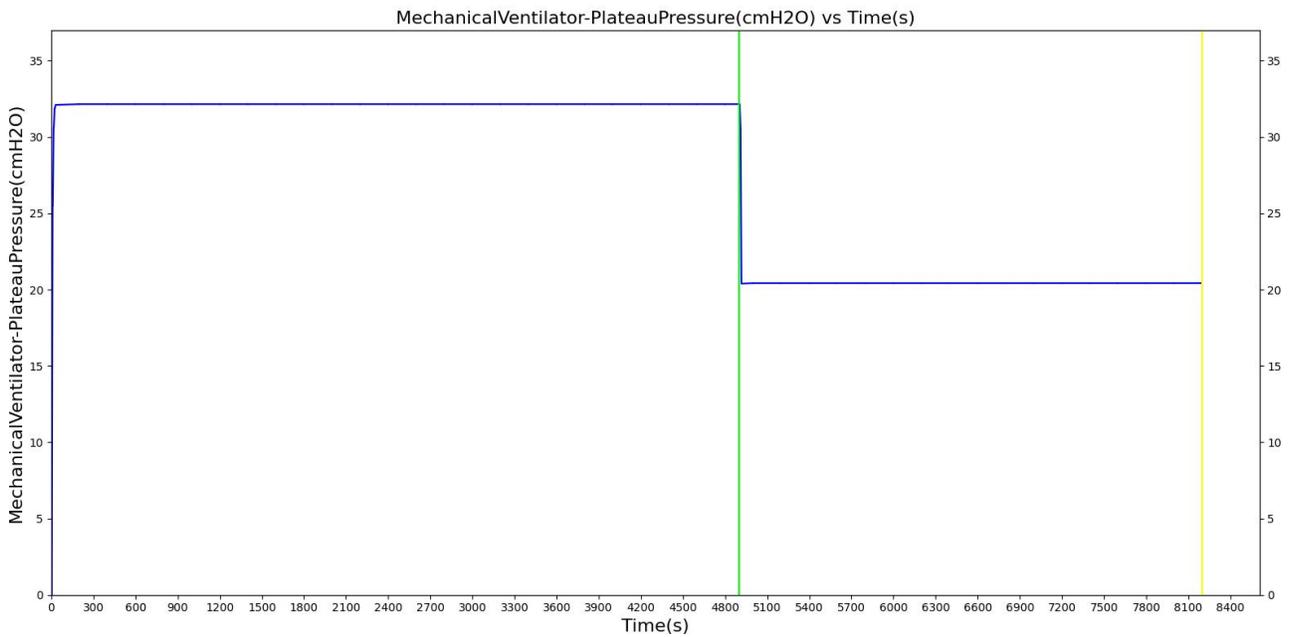**(a)** Tidal volume.
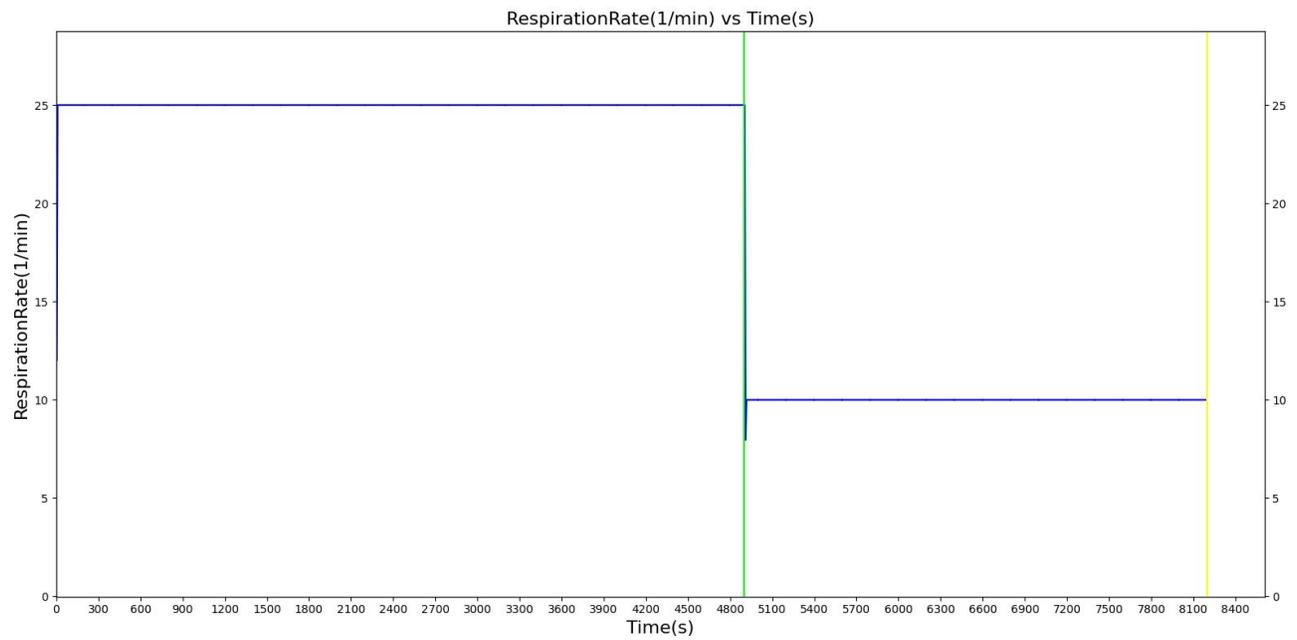
(b) Respiratory rate.

(c) Aortic P_{O_2}.

(d) Aortic P_{CO_2}.
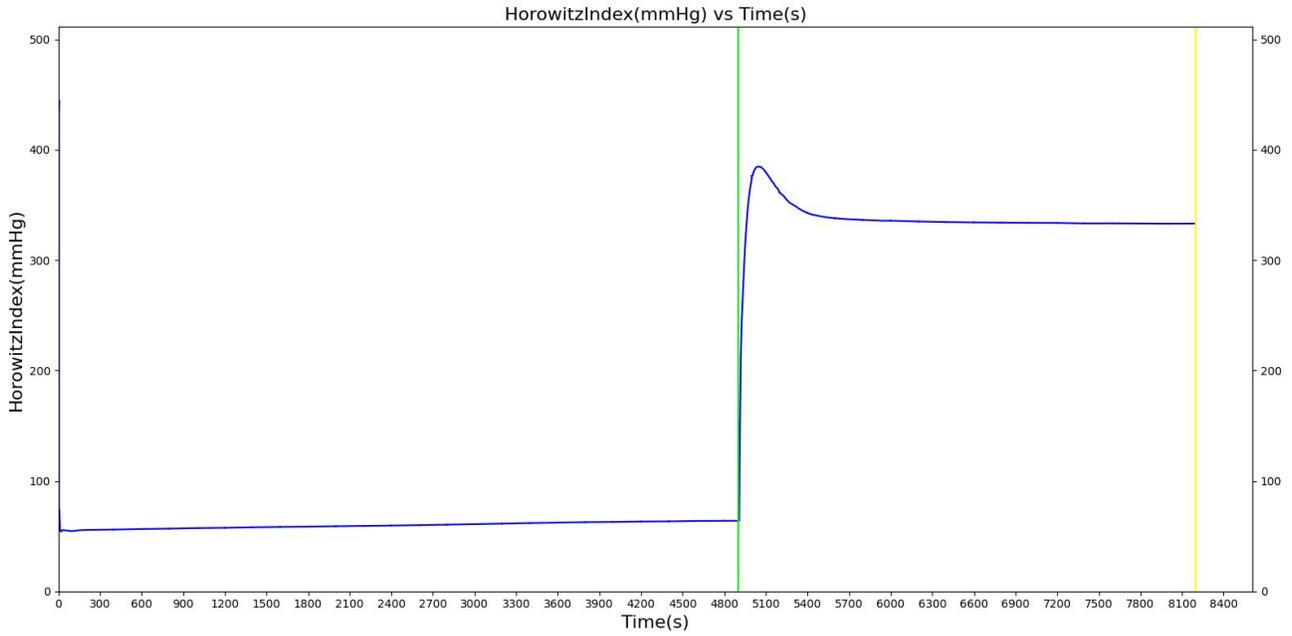
(e) Horowitz index (PaO_2/FiO_2).

(f) Plateau pressure.

Supplementary Figure S2. Select outputs from the titration scenario simulation. At time 0 s, severe ARDS is induced and mechanical ventilation is initiated. After reaching physiologic steady state at 4,900 s, venovenous ECMO is initiated and ventilator settings are adjusted to lung-rest ventilation.