Appendix

  A lumped parameter model (LPM, electric circuit analogies) is used to model hemodynamics in the pulmonary circulation. As shown in Figure 1, both the right atrium (RA) and left atrium (LA) are modeled by a constant pressure source. The pulmonary arteries (PAs) are modeled by three element Windkessel models. The right ventricle (RV) is modeled by a varying compliance. The pressure in the RV is a function of RV volume expressed by a combination of two pressure-volume curves ($EDPVR$ and $ESPVR$) with an activation function a (13). The LPM is governed by an ordinary differential equation (ODE) system (Equations 1-5).

$$\frac{dq_{TC}}{dt} = \frac{U_{RA} - P_{RV} - \Delta P_{TC}}{L_{TC}}; (1)$$

$$\frac{dV_{RV}}{dt} = q_{TC} - q_{PV}; (2)$$

$$\frac{dq_{PV}}{dt} = \frac{P_{RV} - P_{PA} - \Delta P_{PV}}{L_{PV}}; (3)$$

$$\frac{dP_{PA1}}{dt} = q_{PA1}\frac{(R_{P1}+R_{d1})}{(R_{d1}+C_{PA1})} + R_{P1}\frac{dq_{PA1}}{dt} + \frac{U_{LA}}{R_{d1}C_{PA1}} - \frac{P_{PA1}}{R_{d1}C_{PA1}}; (4)$$

$$\frac{dq_{PA2}}{dt} = \frac{P_{PA1}}{(C_{PA2}R_{d2}R_{p2})} + \frac{1}{R_{p2}}\frac{dP_{PA1}}{dt} - q_{PA2}\frac{(R_{P2}+R_{d2})}{(C_{PA2}R_{d2}R_{p2})} - \frac{U_{LA}}{(C_{PA2}R_{d2}R_{p2})}; (5)$$

where variables V, q, P, ΔP and L are volume, flow, pressure, pressure drop across a valve and inductance respectively and constants R, C and U are resistance, capacitance and pressure head. Subscripts TC, RA, RV, PV, LA, PA represent the tricuspid valve, right atrium, right ventricle, pulmonary valve, left atrium and pulmonary artery respectively. In addition, auxiliary functions for the ODE system are given as follows,

$$P_{RV} = (1-a)f_D EDPVR(V_{RV}) + ESPVR(V_{RV}); (6)$$

$$EDPVR = C_1 V_{RV} + C_2; (7)$$

$$ESPVR = C_3 V_{RV} + C_4; (8)$$

$$a = \begin{cases} 2(1-k)\dfrac{mod(t,T_c)}{Ts}, & mod(t,T_c) < \dfrac{Ts}{2} \\[2mm] 1-k+ksin\left(\pi\left(\dfrac{mod(t,T_c)}{T_s}-\dfrac{1}{2}\right)\right), & \dfrac{Ts}{2} < mod(t,T_c) < T_s \\[2mm] 1-sin\left(\dfrac{\pi}{2}\dfrac{mod(t,T_c)-T_s}{T_r}\right), & T_s < mod(t,T_c) < T_s+T_r \\[2mm] 0, & mod(t,T_c) > T_s+T_r \end{cases} ; (9)$$

where f_D, C_1, C_2, C_3, C_4 and k are constant coefficients and a is the activation function. Pressure drops across the tricuspid and pulmonary valves ΔP_{TC} and ΔP_{PV} are given by a valve model proposed by Mynard et al. and shown in Equations 10-18.

$$\Delta P_{TC} = B_{TC}q_{TC}\frac{|q_{TC}|}{L_{PV}}; (10)$$

$$\Delta P_{PV} = B_{PV}q_{PV}\frac{|q_{TC}|}{L_{PV}}; (11)$$

$$B_{TC} = \frac{\rho}{2A_{TC}^2}; (12)$$

$$B_{PV} = \frac{\rho}{2A_{PV}^2}; (13)$$

$$L_{TC} = \frac{\rho l_{TC}}{A_{TC}}; (13)$$

$$L_{PV} = \frac{\rho l_{PV}}{A_{PV}}; (14)$$

$$A_{TC} = (M_{TC}S_{TC} - N_{TC}S_{TC})\zeta_{TC} + N_{TC}S_{TC}; (15)$$

$$A_{PV} = (M_{PV}S_{PV} - N_{PV}S_{PV})\zeta_{PV} + N_{PV}S_{PV}; (16)$$

$$\frac{d\zeta_{PV}}{dt} = \begin{cases} (1-\zeta_{PV})K_{voP}(P_{RV}-P_{PA}), & P_{RV} \geq P_{PA} \\ (\zeta_{PV})K_{vcP}(P_{RV}-P_{PA}), & P_{RV} < P_{PA} \end{cases} ; (17)$$

$$\frac{d\zeta_{TC}}{dt} = \begin{cases} (1-\zeta_{TC})K_{voT}(U_{RA}-P_{RV}), & U_{RA} \geq P_{RV} \\ (\zeta_{PV})K_{vcT}(U_{RA}-P_{RV}), & U_{RA} < P_{RV} \end{cases} ; (18)$$

where variables A_{TC} and A_{PV} are effective areas for the tricuspid and pulmonary valves respectively. The dynamics of valve effective area is described by Equations 17 and 18, where $\zeta = 0$ indicates a closed valve and $\zeta = 1$ indicates a fully open valve. For a normal valve, constants M_{TC} and N_{TC} are set to 1 and 0, respectively. When stenosis or regurgitation presents, $M_{TC} < 1$ or $N_{TC} > 0$ is used to model a stenotic or leaking valve.

A standard Runge-Kutta method is employed to solve Equations 1-5 and 17-18. Pressure-volume loop is obtained by plotting solutions of P_{RV} and V_{RV} in the X-Y plane. In this study, a multi objective optimization (MATLAB, The Mathworks Inc., Natick, MA) is used to identify LPM parameters to match catheterization derived RV pressures (systolic and diastolic) and PA pressures (systolic, diastolic and mean) and MRI derived volumes (end diastolic and end systolic volumes). Typical ranges for optimization parameters and constant LPM parameters are listed in Tables O1 and O2 respectively.

To compare with P-V loops generated by the LPM, RV pressure tracing data and time dependent RV volume curve were processed and plotted in the pressure-volume plane for two patients. The procedure is described as follows. First, RA, RV and PA pressure and EKG signals were extracted from Mac-Lab system (GE Healthcare, Milwaukee, WI) and aligned according to simultaneously recorded ECG signals (R-R interval). Isovolumetric contraction and relaxation are determined by the intersections of RV-PA and RV-RA pressure curves (Figure O2a). Using ECG-gated and breath-held techniques (24), 20 cardiac phases of multi slice cine images were recorded yielding a slice thickness of 8 mm and a temporal resolution of 48 ms. Endocardial borders for the RV were segmented by a radiologist on multiple short-axis planes and RV volumes were calculated for each cardiac phase resulting in a time-dependent RV volume curve. End-systolic and end-diastolic volumes (EDV and ESV) correspond to the smallest and largest points of the RV volume curve. Then the RV volume curve was scaled and aligned with the RV pressure curve based on the end systolic point (Figure O2a). Although no valvular regurgitation was seen, RV volumes were not constant during isovolumetric contraction and relaxation phases largely due to a relatively low temporal resolution and segmentation errors. Therefore, RV volume curves were corrected by imposing constant ESV and EDV during isovolumetric contraction and relaxation phases. Then, a P-V

loop can be obtained by plotting corrected RV volume and pressure data on the P-V plane as shown in Figure 1.

Appendix Table and Figure Legends

Table O1 Typical parameter ranges for optimization. T_c: cardiac cycle time; P_{cath}: catheterization measured pressure (mmHg). R_2, C_{PA2} and R_{d2} are equal to R_1, C_{PA1} and R_{d1} in this study.

Table O2: Constant parameters for LPM. PCW, pulmonary wedge pressure.

Online only Figure O1 Lumped parameter model (LPM) for the right ventricle and pulmonary artery. The LPM is governed by Equations 1-5. Pressures at points a and b are denoted by P_{PA} and P_{PA1}. Flow at point c is denoted by q_{PA2}.
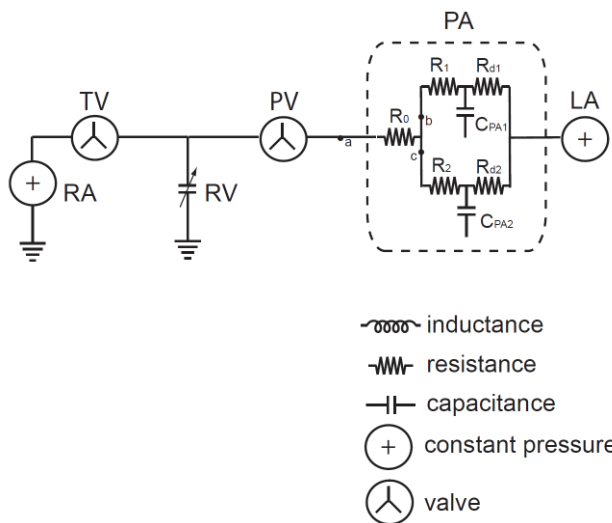
Online only Figure O2: Generation of P-V loops using catheterization pressure tracings and MRI RV volume curves. a) RA (dash line), RV (solid line), PA (dot line) pressure signals were extracted from Mac-Lab recording system and aligned according to ECG signals (R-R interval). The opening and closing times for the pulmonary and tricuspid valves are marked by

black points. A time dependent RV volume curve (dash-dot line) was obtained from multi-slice cardiac cine images in a show axis view and end systolic volume point was aligned with the closing of the pulmonary valve. b) The RV volume curve was corrected by imposing constant volume during isovolumetric contraction and relaxation phases.
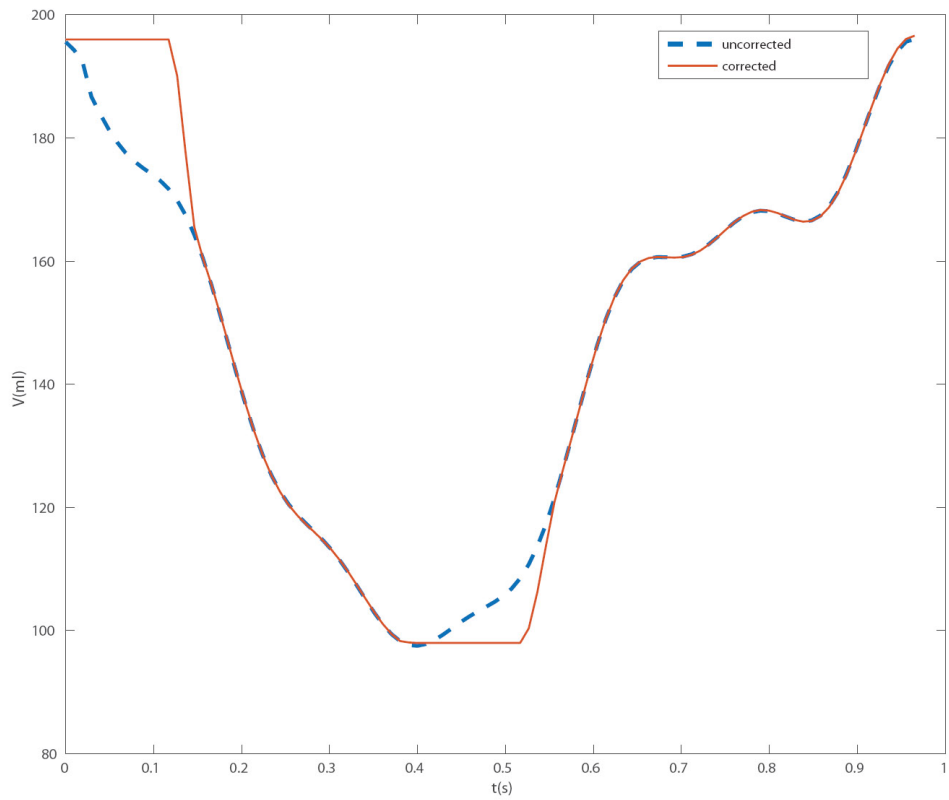
a)
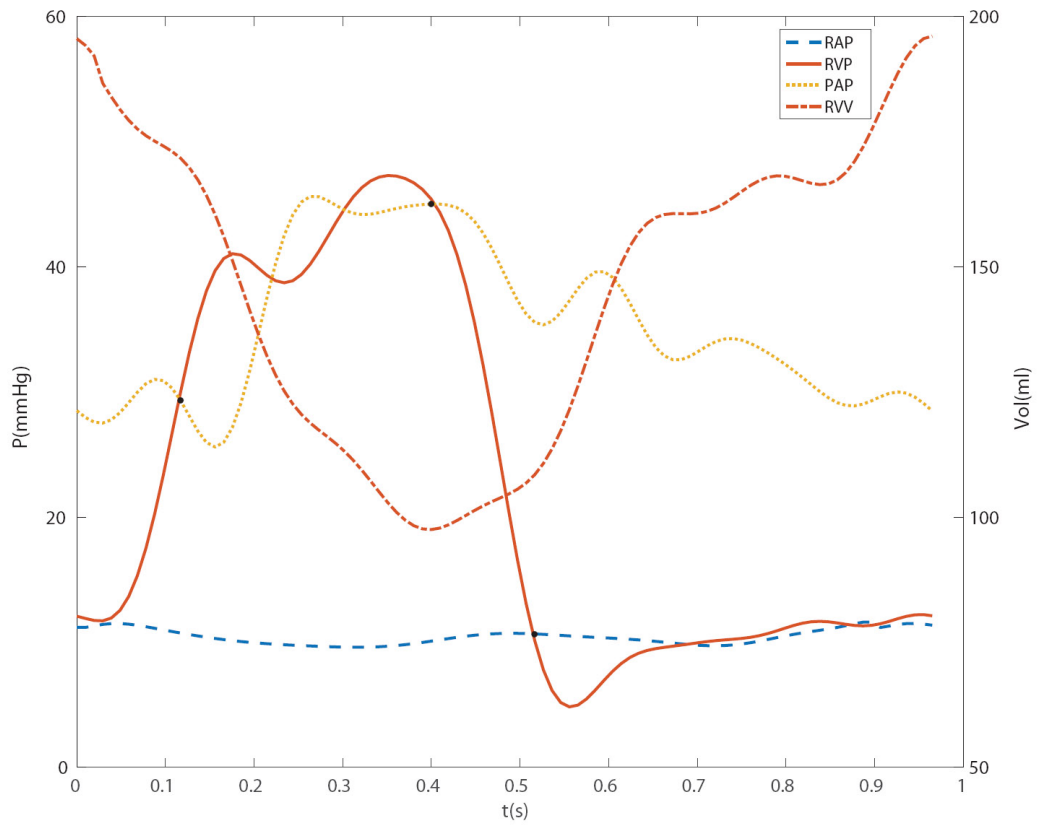
b)

Table O1 Typical parameter ranges for optimization. T_c: cardiac cycle time; P_{cath}: catheterization measured pressure (mmHg). R_2, C_{PA2} and R_{d2} are equal to R_1, C_{PA1} and R_{d1} in this study.

Parameters	Min	Max
T_s	$0.1T_c$	$0.45T_C$
T_r	$0.03T_c$	$0.2T_c$
f_S	0.1	1.5
U_{RA}	P_{cath}-1	P_{cath}+1
C_1	0.01	3.0
C_2	-50	50
C_3	0.01	0.3
C_4	-50	50
R_0	0.01	0.3
R_1	0.01	0.3
C_{PA1}	0.1	0.9
R_{d1}	0.01	2.0

Table O2: Constant parameters for LPM. PCW, pulmonary wedge pressure.

K_{voP}	20.0
K_{vcP}	15.0
K_{voT}	300
K_{vcT}	600
l_{PV}	0.08
A_{PV}	100.0
l_{TC}	0.08
A_{TC}	90.0
U_{RA}	PCW