

## **Supplementary information:**

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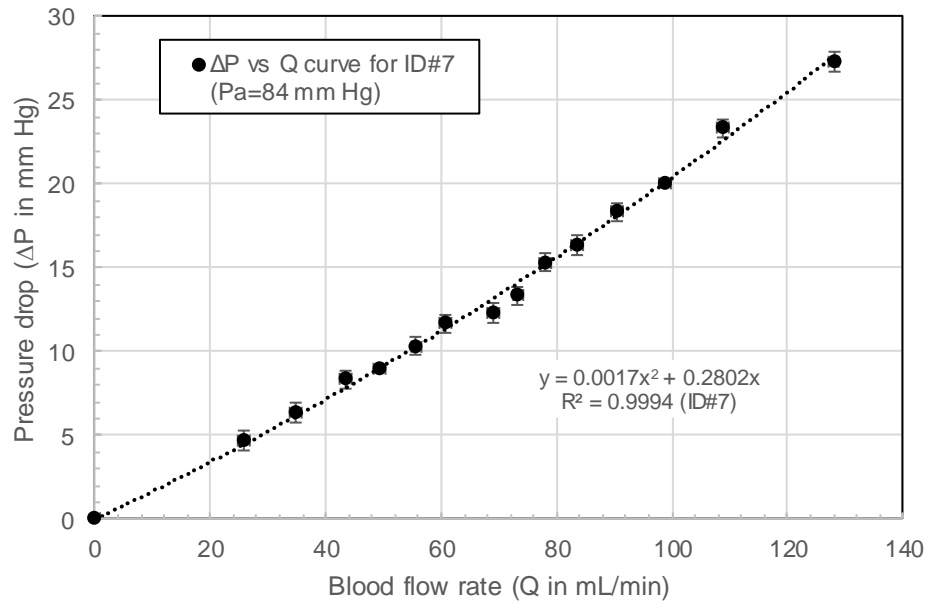
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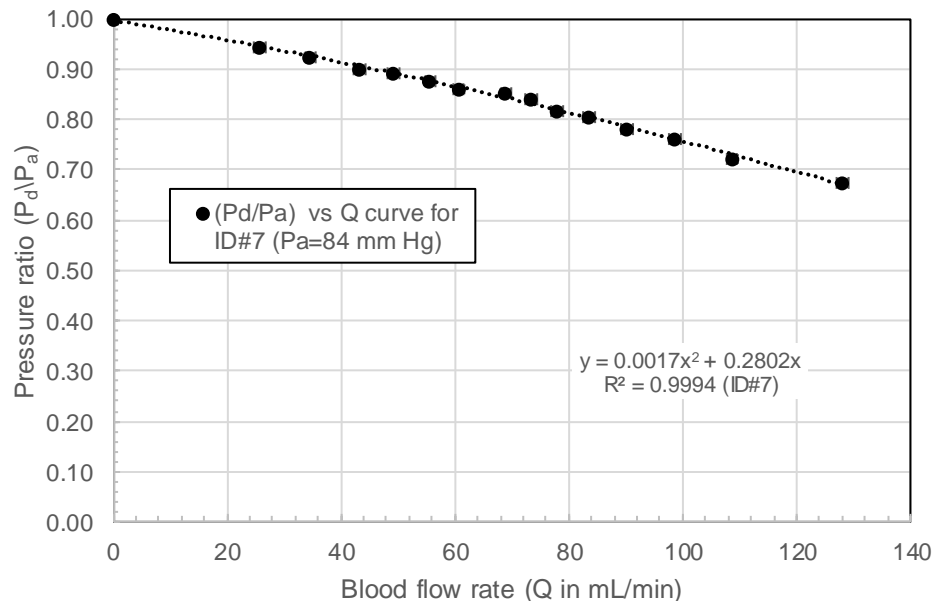
This supplementary file describes the determination of hyperemia from the *in vitro* experiments and thus FFR<sub>3D</sub>.

*Pressure drop- Flow rate Characteristics.* Young et al.<sup>1-4</sup> developed fluid dynamic equations that describe the relationship between the pressure distal to a stenosis and the flow. The  $\Delta P$ -Q characteristics across the stenosis can be expressed as a quadratic relation  $\Delta P = P_a - P_d = A_v Q + B Q^2$ ; where  $A_v$  and  $B$  are the viscous loss along the stenosis and exit loss (due to the change in momentum) coefficients, respectively. When coronary flow increases, the coronary perfusion pressure distal to the stenosis decreases in a nonlinear fashion, according to the equation,  $P_d = P_a - A_v Q - B Q^2$ .

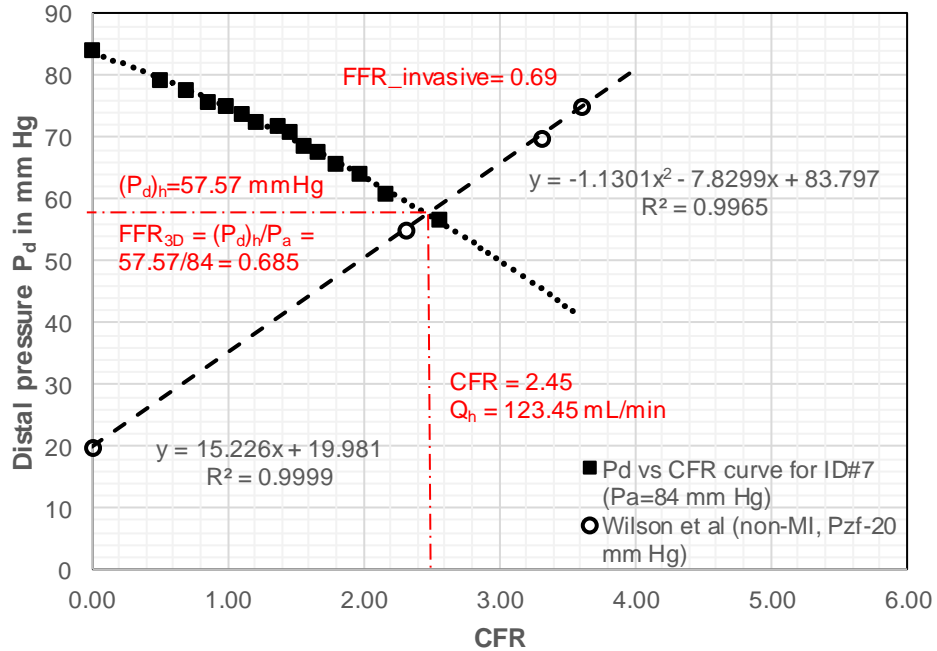
Regression analysis was used to fit a quadratic relationship in the (i) pressure drop ( $\Delta P$ ) – flow rate (Q) and (ii) pressure ratio ( $P_d/P_a$ ) – flow rate (Q) characteristics from the *in vitro* experiment, respectively, as shown in Supplementary Figures 1 and 2. Similarly, as demonstrated in Supplementary Figure 3, linear regression analysis was used to fit a linear curve on the *clinical* hyperemic coronary flow reserve (CFR) – distal pressure ( $P_d$ ) characteristics.



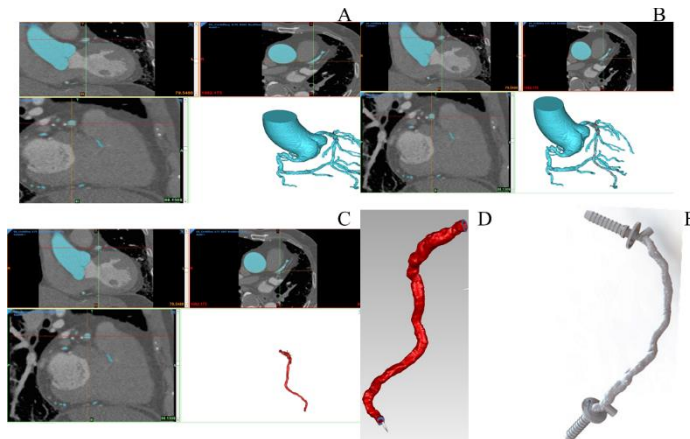
**Supplementary Figure 1:** Pressure drop ( $\Delta P = P_a - P_d$ ) vs flow (Q) characteristics for a 3D printed patient-specific LAD model at fixed aortic pressures of 84 mm Hg (from ICA).  $P_a$ , aortic pressure in mm Hg;  $P_d$ , distal pressure in mm Hg; Q, flow rate in mL/min.



**Supplementary Figure 2:** Pressure ratio vs flow characteristics for a 3D printed patient-specific LAD model at fixed patient-specific aortic pressures of 84 mm Hg (from ICA).  $P_a$ , aortic pressure in mm Hg;  $P_d$ , distal pressure in mm Hg; Q, flow rate in mL/min.



**Supplementary Figure 3:** Pd vs CFR characteristics for a 3D printed patient-specific LAD model at fixed aortic pressures of 84 mm Hg (from ICA). CFR indicates coronary flow reserve;  $P_d$ , pressure distal to stenosis; DS, Pzf, zero-flow mean pressure; Wilson et al<sup>5</sup>



**Supplementary Figure 4:** Comparison of the aorto-coronary and coronary segmented model with the 3D printed part. (A,B) Segmented aortocoronary model in different views (C) extraction of single coronary artery from aortocoronary model (D) remeshing the coronary mesh and thickening it to 1 mm (representative of coronary thickness) (E) 3D model with barbs attached for maintain a leakless watertight fit in the invitro setup

## References:

1. Young DF, Cholvin NR, Kirkeeide RL, Roth AC. Hemodynamics of arterial stenoses at elevated flow rates. *Circ Res* 1977;**41**(1):99-107.
2. Young DF, Cholvin NR, Roth AC. Pressure drop across artificially induced stenoses in the femoral arteries of dogs. *Circ Res* 1975;**36**(6):735-43.
3. Young DF, Tsai FY. Flow characteristics in models of arterial stenoses. I. Steady flow. *J Biomech* 1973;**6**(4):395-410.
4. Young DF, Tsai FY. Flow characteristics in models of arterial stenoses. II. Unsteady flow. *J Biomech* 1973;**6**(5):547-59.
5. Wilson RF, Johnson MR, Marcus ML, Aylward PE, Skorton DJ, Collins S, White CW. The effect of coronary angioplasty on coronary flow reserve. *Circulation* 1988;**77**(4):873-85.