JHTD-23-26131

Canary in the Cardiac-Valve Coal Mine: Flow Velocity and Inferred Shear during Prosthetic Valve Closure – Predictors of Blood Damage and Clotting

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Received: 16-Aug-2023, Manuscript No. JHTD-23-26131; **Editor assigned:** 18-Aug-2023, PreQC No. JHTD-23-26131 (PQ); **Reviewed:** 01-Sep-2023, QC No. JHTD-23-26131; **Revised:** 11-Jan-2025, Manuscript No. JHTD-23-26131 (R); **Published:** 18-Jan-2025, DOI: 10.35248/2329-8790.25.13.646

Citation: Scotten LN, Siegel R, Blundon DJ, Deutsch MA, Martin TRP, Dutton JW, et al. (2025) Canary in the Cardiac-Valve Coal Mine: Flow Velocity and Inferred Shear during Prosthetic Valve Closure – Predictors of Blood Damage and Clotting. J Hematol Thrombo Dis. 13.646.

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SUPPLEMENTARY APPENDIX

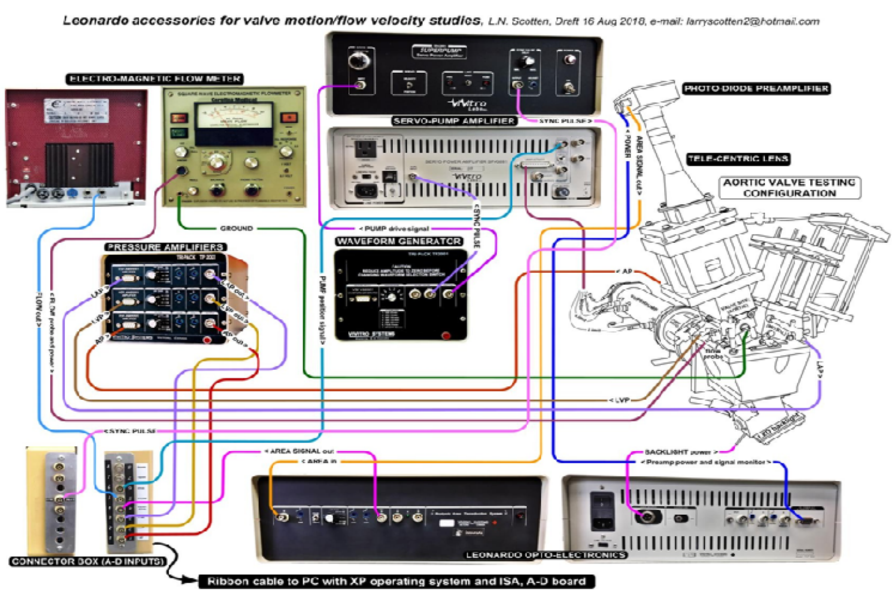

Figure S1: Electrical inter-connections for testing aortic valves.

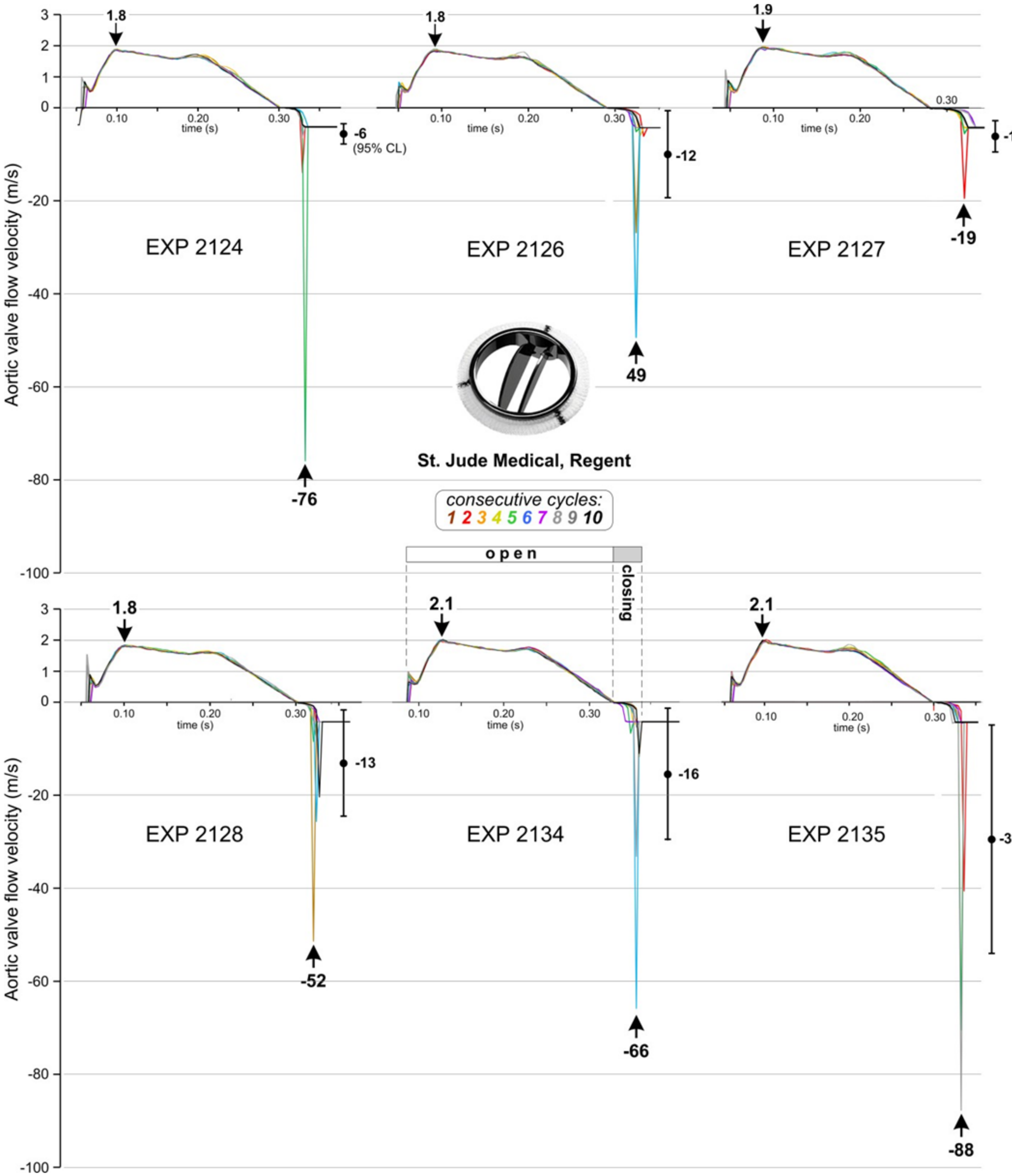

Figure S2: Laboratory data of AORTIC valve flow velocities over 10 consecutive cycles, average, and 95% Confidence Limits (CL). Importantly, negative flow velocity transients during valve closing substantially exceed the maximum positive valve open forward flow velocities. Results challenge the persisting bias towards open valve performance as the primary factor in valve-induced thrombogenic complications.

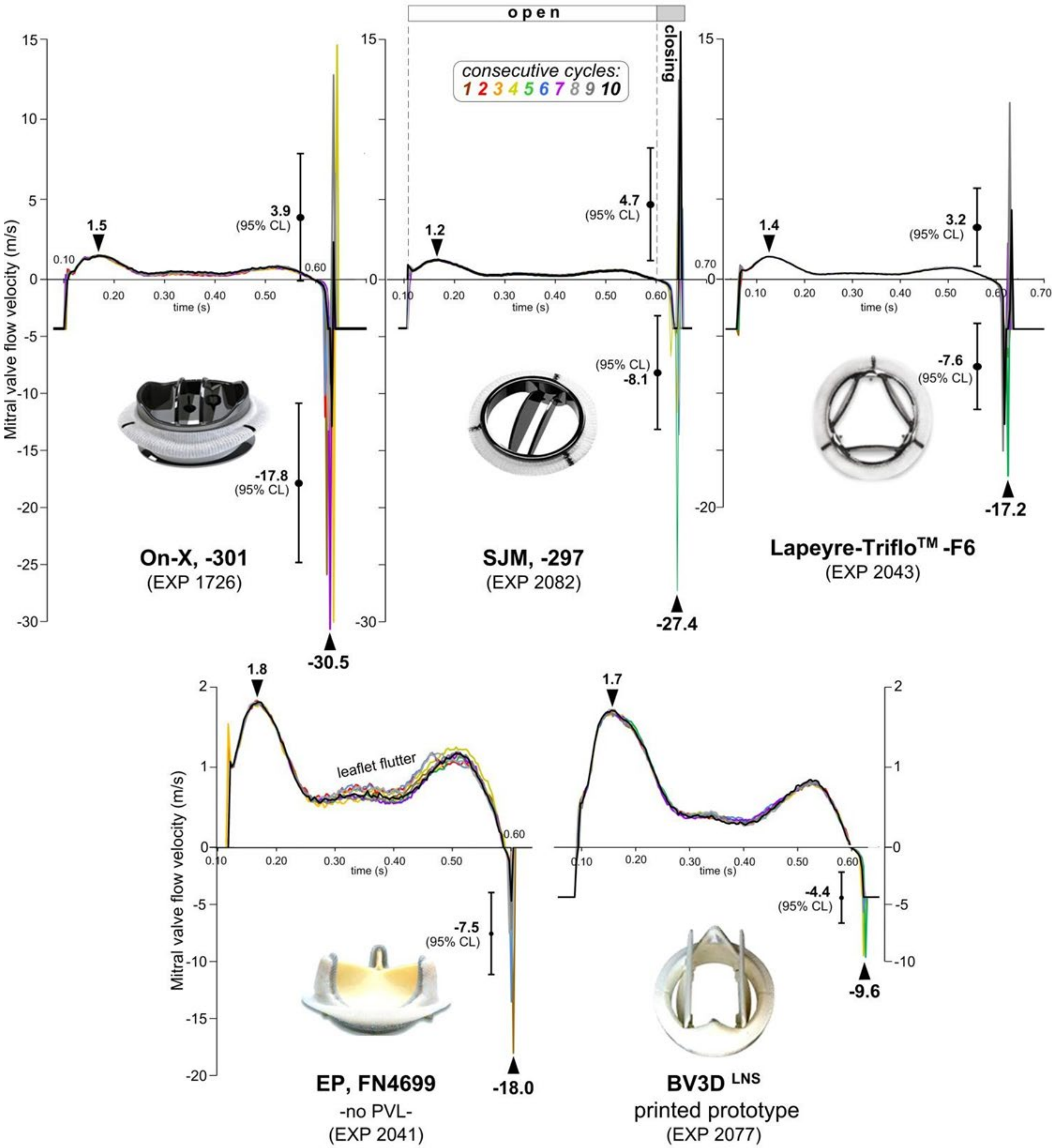

Figure S3: Laboratory data of MITRAL valve flow velocities over 10 consecutive cycles, average, and 95% Confidence Limits (CL). Importantly, flow velocity transients during valve closing and rebound substantially exceed the maximum positive valve open flow velocities. Results challenge the persisting bias towards open valve performance as the primary factor in valve-induced thrombogenic complications.

S4 Video

See MPEG 4, animated visualization of prototype BV3D valve structures and full range motion potential. https://youtu.be/5QmDPbfUvTM

S5 Reduced-order models

Figure 1 depicts Leonardo pulse duplicator system with reduced-order electrical models for the Viscoelastic Impedance Adapter (VIA) and outflow loading comprised of resistive and compliance elements used in the pulsed duplicator and assigned in computational fluid- structure simulations with saline used as the test fluid.

Upstream VIA elements immersed in water:

C_{VIA1} = 0.0010 mL/mm Hg; 0.0275 mmHg mL^{-1}; C_{VIA2} = 0.1456 mL/mm Hg; 0.0347 mmHg mL^{-1}

R_{VIA} = 0.15 mm Hg/mL/s; 0.15 mm Hg $mL^{-1}s^{2}$; and R_{out} = 0.0898 mm Hg $mL^{-1}s$.

Downstream elements:

R_c = 0.0218 mm Hg $mL^{-1}s$; R_p = 1.31 mm Hg $mL^{-1}s$; and C = 1.27 mm Hg mL^{-1}.

The test fluid is saline.

S5 Compliance and resistance:

A three-element (R–C–R) Windkessel model characterizes the upstream driving and downstream loading conditions specified in resistance and compliance units:

Upstream:

C_{VIA1} = 0.0275 mm Hg mL^{-1}, C_{VIA2} = 0.0347 mm Hg mL^{-1},

R_{VIA} = 0.15 mm Hg $mL^{-1}s$, and R_{out} = 0.0898 mm Hg $mL^{-1}s$

Downstream:

R_c = 0.0218 mm Hg $mL^{-1}s$, R_p = 1.31 mm Hg $mL^{-1}s$, and C = 1.27 mm Hg mL^{-1}

Mathematically, compliance is defined as the ratio of change in air volume to change in air pressure and is considered a bulk modulus of elasticity or young's modulus of air (E):

$$C = 1/E \text{ (in SI units of dyn/cm)}$$

Compliance is modeled by four enclosed air volumes:

$$C_{VIA1} = 120 \text{ ml } (0.0010 \text{ mL/mm Hg})$$

$$C_{VIA2} = 50 \text{ ml } (0.1456 \text{ mL/mm Hg})$$

$$(C_{root}) = 640 \text{ mL Aortic root}$$

$$C_{per} = 615 \text{ ml Systemic arterial compliance}$$

Compressibility of air is calculated by a bulk modulus (K):

$$K = 1333.2 \times V\Delta P / \Delta V \approx 140 \text{ kPa}^{-1} \text{ for standard air conditions}$$

Where:

Given that K ≈ 140 kPa^{-1} for standard air conditions,

Check that calculated K is to this approximate value.

V is initial contained air volume (cm^3)

ΔP is the change in contained air pressure (mmHg)

ΔV is the resulting change in contained air volume (cm3)

Conversion factor: 1 mmHg =1333.2 dynes/cm^2

The bulk pump source compliances simulated in VIA contain two air volumes C_{VIA1} and C_{VIA2}. These volumes are adjustable and cover physiological range. The nominal air volume settings used for valve testing are:

C_{VIA1} = 120 ml (0.0010 mL/mm Hg);

C_{VIA2} = 50 ml (0.1456 mL/mm Hg);

Aortic root (C_{root}) = 640 mL and systemic arterial compliance

C_{per} = 615 mL.

Compliance is defined as the ratio of volume change to pressure change as follows:

$$\text{Compliance} = \frac{\Delta V}{\Delta P \bullet 1333.2}$$

Where:

ΔV = change in contained air volume in ml

ΔP = change in pressure (mm Hg) caused by volume change V

$\Delta P = P_2 - P_1$

P_1 = initial static pressure in mmHg

P_2 = final static pressure in mmHg

Conversion factor: 1 mmHg = 1333.2 Dynes/cm^2

Air volume$_{max}$ values found experimentally that simulate left ventricle, aortic root, and systemic arterial compliance and also calibrated parameters for the reduced-order models using saline as a test fluid facilitated realistic pressure and flow wave forms while under pulsatile flow conditions were:

- R_{VIA} = 0.15 mm Hg/mL/s.
- Aortic root C_{VIA1} = 120 ml = 0.1456 mL/mm Hg
- Output compliance C_{VIA2} = 50 ml
- Aortic root C_{root} = 640 ml= 0.0010 mL/mm Hg
- Left ventricle source compliance air volume C_{VIA2} = 640 ml
- Output compliance air volume = 50 ml
- Peripheral systemic C_{per} = 615 ml

Resistance:

Resistance to flow causes frictional loss of energy and flow container chamber radius is the dominant determinant of resistance. In Figure 1, R_{VIA} and R_{per} offer flow resistance. R_{VIA} consists of a micro-porous water filter section which offers a low fixed resistance to flow (200 c.g.s. units). The peripheral resistance R_{per} offers alterable resistance allowing for operator adjustment of end diastole aortic pressure.

Light source

Phlox® SLLUB Backlight** 50 × 50mm × 8.5 mm, LED back light source (diffuse red), luminance 5,780 cd/m^2, uniformity 99.24%, wavelength 625 ± 15 nm.

**PHLOX Corp., ZAC de l'Enfant, Aix-en-Provence, France

Figure S6: A mining tradition dating back to 1911 used canaries in coal mines to detect carbon monoxide and other toxic gases before they hurt humans. In 1906, Dr. John Scott Haldane proceeded to study asphyxia in coal miners in coal miners and proposed that "miners carry small animals like mice or canaries to detect levels of gas in their working environment" This practice was in vogue until 1986. (Sekhar KC, Rao SC. John Scott Haldane: The father of oxygen therapy. Indian J Anaesth. 2014;58:350-352).

Leonardo^{LNS} test system specifications:

- Temporal resolution ≈ 1.04 μs;
- POVA spatial resolution * ≈ 0.34 mm^2;
- Telecentric lens maintains constant magnification ≈ 0.16 ×;
- Working distance ≈ 18 cm;
- Perspective error <0.3% (depth 15 mm);
- Spatial sensitivity variation <6%;
- LED back light (red):
- Wavelength 625 nm, ± 15 nm;
- Uniformity 99.24%;
- Luminance 5,780 cd/m^2;
- Typical linear calibration: y=0.00128x, with R^2=0.9998.

*Photodiode (Hamamatsu S1723-06) highly resolves spatial features of imaged backlit valve area. With zero input light conditions, the opto-electronic system noise level measures ~3.2 mV_{rms}.

S7 Spatial area resolution of photo diode

Photodiode approach:

We use a photo diode capable of high resolution sensing of POVA. It has a low noise level of approximately 3.2 mV_{rms} measured under zero light conditions. The photo diode's light-sensitive area is 10 mm × 10 mm. Optics are chosen to achieve a magnification of ~0.16 ×. The image of the backlit valve is focused onto the photodiode creating an image ~6 mm diameter (area of ~0.28 cm^2). A black paper mask with a 7 mm diameter aperture is placed on the front window surface of the photodiode. The purpose of the mask is to prevent extraneous light reflections in the optics from reaching the photo diode, enhancing the accuracy of measurements. The spatial area resolution =

Dark noise (3.2 mV_{rms}) × calibrated opto-electronics POVA sensitivity (0.106 mm^2/mV_{rms}) = 0.34 mm^2