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Using Discrete Multi-Physics for studying the dynamics of emboli in flexible venous valves

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Abstract

Emboli, which are parts of blood clots, can be stuck in the vasculature of various organs (most frequently, lungs) and cause their malfunction or even death. In this work, using mathematical modelling, different types of emboli-like structures are studied in a double venous valve system. The model is implemented with a fully Lagrangian Discrete Multi-Physics technique and the flow is governed by flexible walls. The study shows the effect of different diameters and lengths of a free embolus in the flow surrounding the valve. The presence of an embolus strongly affects the dynamics of both the fluid and the leaflets in venous valves and the permanence of the embolus in the valve chamber is narrowly linked with its length.

Keywords: Discrete Multi-Physics, Smoothed Particle Hydrodynamics, Mass and Spring Model, biological venous valve, Emboli, Deep Venous Thrombosis.

20 **1. Introduction**

21 An embolus is generally formed when a section of a thrombus detaches and circulates in the
22 cardiovascular system until reaching narrow vessels, most frequently, in the lungs [1-3].
23 When emboli are trapped, they can obstruct blood flow in the lungs leading to a potentially
24 life-threatening complication known as pulmonary embolism (PE) or deep vein thrombosis
25 (DVT). In the UK alone, around 25,000 deaths are caused by PE or DVT; this number is five
26 times higher than those from breast cancer, AIDS and road accidents combined [4].

27 While medical research highlights the role of DVT on the hydrodynamics around venous
28 valves [5], the actual physical interaction of the embolus with the valve remains unexplored.
29 The literature provides a wide range of publications about venous and arterial thrombosis, but
30 the majority of these studies focuses on thrombogenesis and clotting [6-14], rather than the
31 dynamics of the embolus.

32 To circumvent the current limitations of in-vivo and in-vitro models, computer simulations
33 (in-silico modelling) of the the venous valve have been carried out but, with a few exceptions
34 [13, 15, 16], emboli are not accounted for. For DVT however, this represents a serious
35 limitation since the presence of the embolus changes considerably the hydrodynamics around
36 the valve.

37 Previous studies [15, 16] have shown that the diameter, the elasticity and the location of an
38 embolus affect the flow in arterial bifurcations [15] or in Inferior Vena Cava (IVC) [16]. But
39 the interaction of the embolus with more complex settings such as the flexible leaflets of the
40 venous valve has not been investigated. Only Simão et Al. [13] consider the presence of solid

41 particles in the venous valve, but these are simple Lagrangian point particles and the flow,
42 therefore, is not fully resolved around them.

43 By modelling the physical interaction of emboli with different shapes and flexibilities with
44 the soft leaflets of the venous valve and the change of hydrodynamics that this involves, this
45 paper fills a gap in the literature since the valve environment is probably the most critical for
46 DVT and the presence of clots in the vicinity of the valve has been associated with the
47 occurrence of new thrombosis activation sites [5].

48 **2. Methodology**

49 **2.1. Modelling**

50 A hybrid approach, based on a particle framework, is implemented to model haemodynamics
51 and solid structure deformation. The technique, called Discrete Multi-Physics (DMP) [14, 17,
52 18], associates Smoothed Particle Hydrodynamics (SPH) [19-21] and the Mass and Spring
53 Model (MSM) [22-24] and has been used to model the fluid-structure interactions occurring
54 in deep vein valves [14], cardiac valves [17] and the intestine [18].

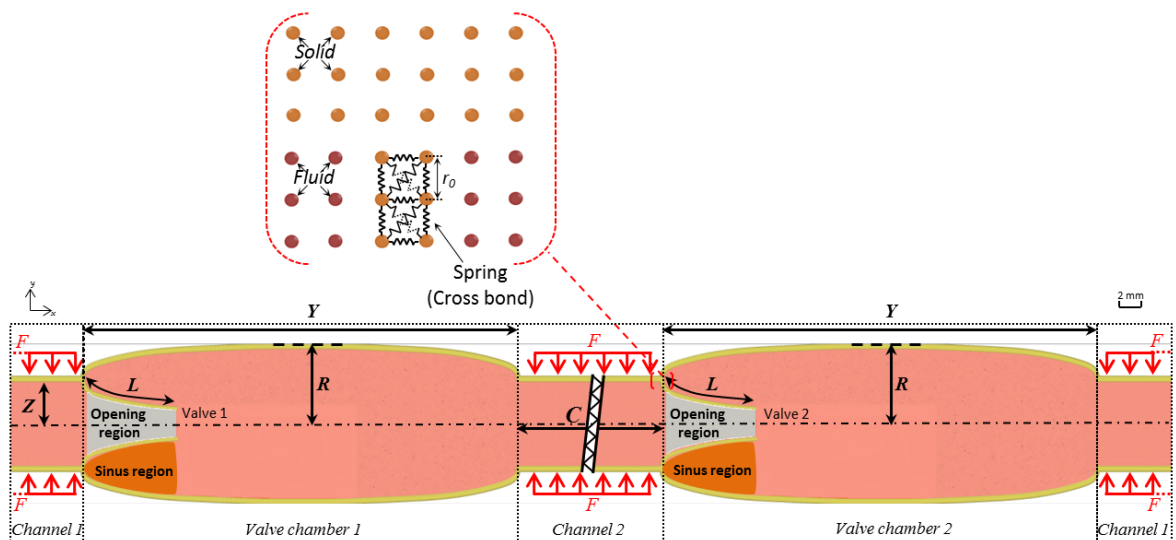
55 In this approach, the liquid is represented by SPH particles that interact with each other by
56 viscous and pressure forces and the tissues by MSM particles inter-connected by means of
57 computational springs (to model the elastic modulus) and dashpots (to model viscoelasticity).
58 The essential ideas behind the DMP method are summarized in Appendix A; the reader can
59 refer to [24] for a more extensive explanation of the DMP theory and to [22] for applications
60 in different fields such as lava flows, cell dynamics and solid-liquid flow.

61 **2.2. Geometry**

62 In this study, we use a 2D schematic representation of a double leg venous valve system. The
63 geometry is similar to the short valve model [14] but here it is used with two antagonist
64 valves (Fig. 1). The channel radius is $Z = 0.004$ m, the membrane length is $L = 0.01$ m, the
65 radius of the valve chamber is $R = 0.007$ m and its length is $Y = 0.04$ m [14]. The two valve
66 systems are inter-connected and the total length between the two chambers is $C = 0.048$ m
67 (0.046 m in [25]). The external walls are divided into four parts: two flexible sections where
68 an external force is applied (Channel 1 and Channel 2 in Fig. 1), and two valve chambers

69 (Valve chamber 1 and Valve chamber 2 in Fig. 1) that contain the leaflets. Since periodic
 70 boundary conditions are enforced, the fluid exiting from the channel opening on the right is
 71 reinserted to the channel opening on the left and vice versa. For the same reason, Channel 1 in
 72 Fig. 1 appears to be divided into two sections (one on the left and another on the right), but,
 73 computationally, the two ends are joined together by the periodic boundary conditions. A net
 74 fluid flow is achieved by means of external forces acting alternatively on Channel 1 and
 75 Channel 2 (Fig. 1). When a ‘squeezing’ force F (see Fig. 1) is applied to Channel 1, Valve 1
 76 opens, Valve 2 closes, and the fluid flows from the left to the right. When F is applied to
 77 Channel 2, Valve 2 opens, Valve 1 closes, and the fluid maintains the same direction from the
 78 left to the right. This approach mimics the actual motion of blood in the legs’ veins induced
 79 by the contraction of the surrounding muscles.

80 In the rest of the paper, we refer to the regions between the leaflets (in both Valve 1 and
 81 Valve 2) as the ‘opening regions’ and to the regions between the walls and the leaflets (in
 82 both Valve chamber 1 and Valve chamber 2) as ‘sinus regions’ (Fig. 1).



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Fig. 1. Illustration of the double venous valve 2D geometry.

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According to the DMP approach (see Appendix A) both the fluid and the solid are represented by discrete computational entities, which we call ‘fluid particles’ and ‘solid particles’. The different behaviour of fluid and solid particles depends on the type of forces the DMP algorithm applies to each computational particle. If these forces model the viscous and pressure forces commonly acting on fluids, the computational particle behaves like a fluid; if they model the viscoelastic forces acting on solid, the particle behaves like a solid. Computationally, the fluid forces are calculated with the SPH method while the solid forces particles by means of springs (MSM model) as detailed in Appendix A. The wall delimiting the valve chamber is considered stationary and, therefore, no forces are applied to the computational particle representing this part of the domain. Solid-liquid boundary conditions are also modelled by means of inter-particle forces that model no-penetration and no-slip conditions as explained in Appendix A.

2.3. Model parameters

In our simulations, the geometry is divided into 168676 particles spaced of 10^{-4} m: 584 for the valves, 10722 for the walls, and 157370 for the fluid area. As mentioned, SPH particles are used for the fluid, stationary (solid) particles for the valve chamber walls and MSM particles for the flexible walls and the leaflets. Three layers of particles are used for the walls and two for each leaflet, with thicknesses of $3 \cdot 10^{-4}$ m and $2 \cdot 10^{-4}$ m, respectively. The flow is laminar [13, 25, 26] and blood is here considered a Newtonian fluid [15, 27]. Table 1 gathers all the parameters used in the simulation.

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Table 1. Model parameters used in the simulations.

SPH (Eqs. A.5–A.7)	
Parameter	Value
Number of SPH wall particles (3 layers)	10722
Number of SPH valve particles (2 layers)	584 (146 particles/leaflet)
Number of SPH fluid particles	157370
Mass of each particle (fluid)	$1.05 \cdot 10^{-5}$ kg
Mass of each particle (solid)	$2 \cdot 10^{-5}$ kg
Initial distance among particles Δr	$1 \cdot 10^{-4}$ m
Smoothing length h	$2.5 \cdot 10^{-4}$ m
Artificial sound speed c_0	10 m s ⁻¹
Density ρ_0	1056 kg m ⁻³
Viscosity μ_0	0.0035 Pa s
Time step Δt	10^{-6} s
Force F	0.008 N
MSM (Eqs. A.10)	
Parameter	Value
Hookian coefficient k_b (Wall)	$1 \cdot 10^5$ J m ⁻²
Hookian coefficient k_b (membrane)	$5 \cdot 10^6$ J m ⁻²
Viscous damping coefficient k_v (Wall)	1 kg s ⁻¹
Viscous damping coefficient k_v (membrane)	0.1 kg s ⁻¹
Equilibrium distance r_0	$1 \cdot 10^{-4}$ m
BOUNDARIES (eq. A.14)	
Constant K	$4 \cdot 10^{-4}$ J
Repulsive radius r^*	$1 \cdot 10^{-4}$ m

108 2.4. Simulation parameters

109 As detailed in Appendix A, the structure of the flexible tissue (wall and valve) and its
110 elasticity are implemented with a spring model. The spring constant k_b has been chosen in
111 order to model the different elastic properties of the leaflets and the walls (Table 1). A viscous
112 coefficient (k_v) is also added to the MSM springs to confer viscoelastic properties to the valve
113 and the flexible wall as in a Kelvin–Voigt material.

114 The inlet/outlet of the fluid in the x -direction is controlled using periodic boundary conditions.
115 The flow is pulsed periodically and generates several opening and closing of the valves.
116 Therefore, we use the term “cycle” to define a single period including one opening and one
117 closing of the same valve [25, 26]. For each cycle, we model the opening phase by applying a
118 vertical force F (Y -axis) on Channel 2 for 1.5 s while no force is applied to Channel 1 (Fig.
119 1). During the closing phase (1.5 s), Channel 2 is relaxed (F on Channel 2 is set to 0) and F is
120 applied to Channel 1. The force F is constant and uniform for each cycle (Table 1). For all
121 simulations, a total of 10 cycles (30 s) are calculated.

122 **2.5. Emboli**

123 A solid, embolus-like structure is introduced into the flow. The solid particles of the embolus
124 are joined together by springs whose Hook constant is reported in Table 2. Differently from
125 some of our previous studies [14, 17] where the embolus grows due to an aggregation
126 algorithm, here the embolus size is fixed during the simulation.

127 The effect of size, length and embolus’ flexibility is investigated (Table 2). In the literature,
128 no standard size or length for emboli is given and the shape mostly depends on the
129 surrounding flow, channel diameter and valve characteristics [13]. In this work, to account for
130 a variety of potential cases, the selected sizes are in the range used by [16] and the lengths
131 coincide with the length of (i) the sinus region (embolus L6 in Table 2), (ii) half of the valve
132 chamber (embolus L19), (iii) the valve chamber (embolus L37) and (iv) the valve chamber +
133 half of the channel (embolus L77).

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Table 2. Simulation parameters used for the embolus aggregate.

Variation of the diameter of the embolus (spherical) with $k_b = 1 \cdot 10^4 \text{ J m}^{-2}$		
Diameter of the embolus [m]	Location at t = 0 s	Case
$2.6 \cdot 10^{-3} \text{ m}$	Centre of the tube	D26
$5.2 \cdot 10^{-3} \text{ m}$	Centre of the tube	D52
$7.8 \cdot 10^{-3} \text{ m}$	Centre of the tube	D78
Variation of the length of the embolus with height = $2.6 \cdot 10^{-3} \text{ m}$ and $k_b = 1 \cdot 10^4 \text{ J m}^{-2}$		
Length of the embolus [m]	Location at t = 0 s	Case
$5.9 \cdot 10^{-3} \text{ m}$	Sinus region	L6
$19 \cdot 10^{-3} \text{ m}$	Sinus region	L19
$21 \cdot 10^{-3} \text{ m}$	Centre of the tube	L21
$37 \cdot 10^{-3} \text{ m}$	Sinus region	L37
$77 \cdot 10^{-3} \text{ m}$	Sinus region	L77
Variation of the flexibility of the embolus (spherical) with diameter = $7.8 \cdot 10^{-3} \text{ m}$		
Bond coefficient $k_b \text{ [J m}^{-2}\text{]}$	Location at t = 0s	Case
$1 \cdot 10^3 \text{ J m}^{-2}$	Centre of the tube	F103

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3. Results and discussion

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3.1. Hydrodynamics

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A typical simulation without the embolus is shown in Fig. 2. During the opening phase (of

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Valve 1), when F is applied to Channel 1, the pressure in Channel 1 increases; Valve 1 opens

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and Valve 2 closes (Fig. 2a and Fig. 2b). Part of the fluid leaves Channel 1 and accumulates

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in Channel 2, which dilates. During the closing phase (of Valve 1), the force F is applied to

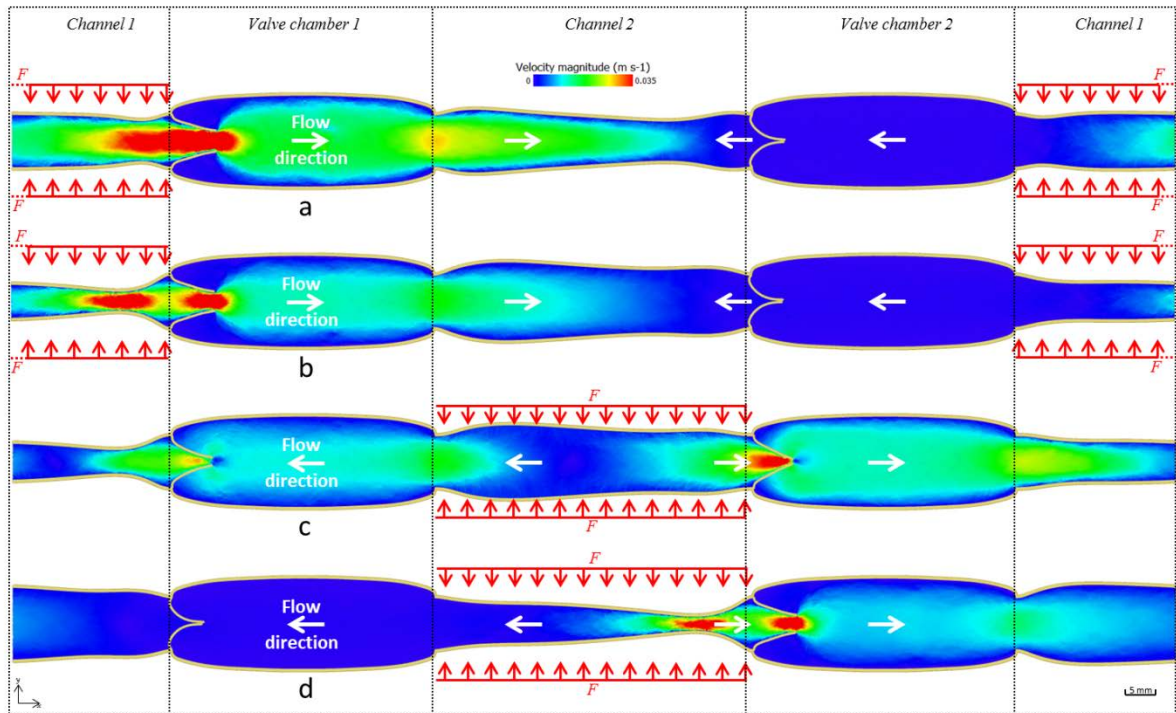
144

Channel 2 and Channel 1 relaxes (F is set to 0). Valve 1 closes while Valve 2 opens (Fig. 2c

145 and Fig. 2d). The contraction and, therefore, the force applied to the vein walls accounts for
146 the level of physical activity of a specific individual. The force used in this study generates a
147 peak blood velocity around 0.035 m s^{-1} which corresponds to a low level of physical activity
148 [13, 14]. This condition was chosen since the risk of DVT increases when the level of
149 physical activity is low.

150 The valve opening-closing mechanism in relation to the contraction of the veins around the
151 valve is confirmed by the available literature [14, 25, 26]. At the time of maximal contraction,
152 however, the vein assumes an asymmetrical shape shown in Fig. 2d. This is probably due to
153 the fact that, in our model, the segments of veins (Channel 1 and Channel 2) connecting two
154 valves are considerably shorter than in reality. The asymmetrical shape can neither be
155 confirmed nor disproved by available visualization data. This circumstance, however, has
156 little relevance to our work, which focuses on the dynamics of the valves rather than that of
157 the veins.

158



159

160 Fig. 2. Valve deformation and velocity magnitude of the system during a cycle: (a) $t = 0$ s, (b)
 161 $t = 0.75$ s, (c) $t = 1.5$ s, (d) $t = 2.25$ s, (e) $t = 3$ s.

162 In the next section, we introduce an embolus-like structure both in the main flow (opening
 163 region in Fig. 1) and behind the valve (sinus region in Fig. 1). The goal is to show how the
 164 presence of a free embolus impacts the flow in the vicinity of the valve.

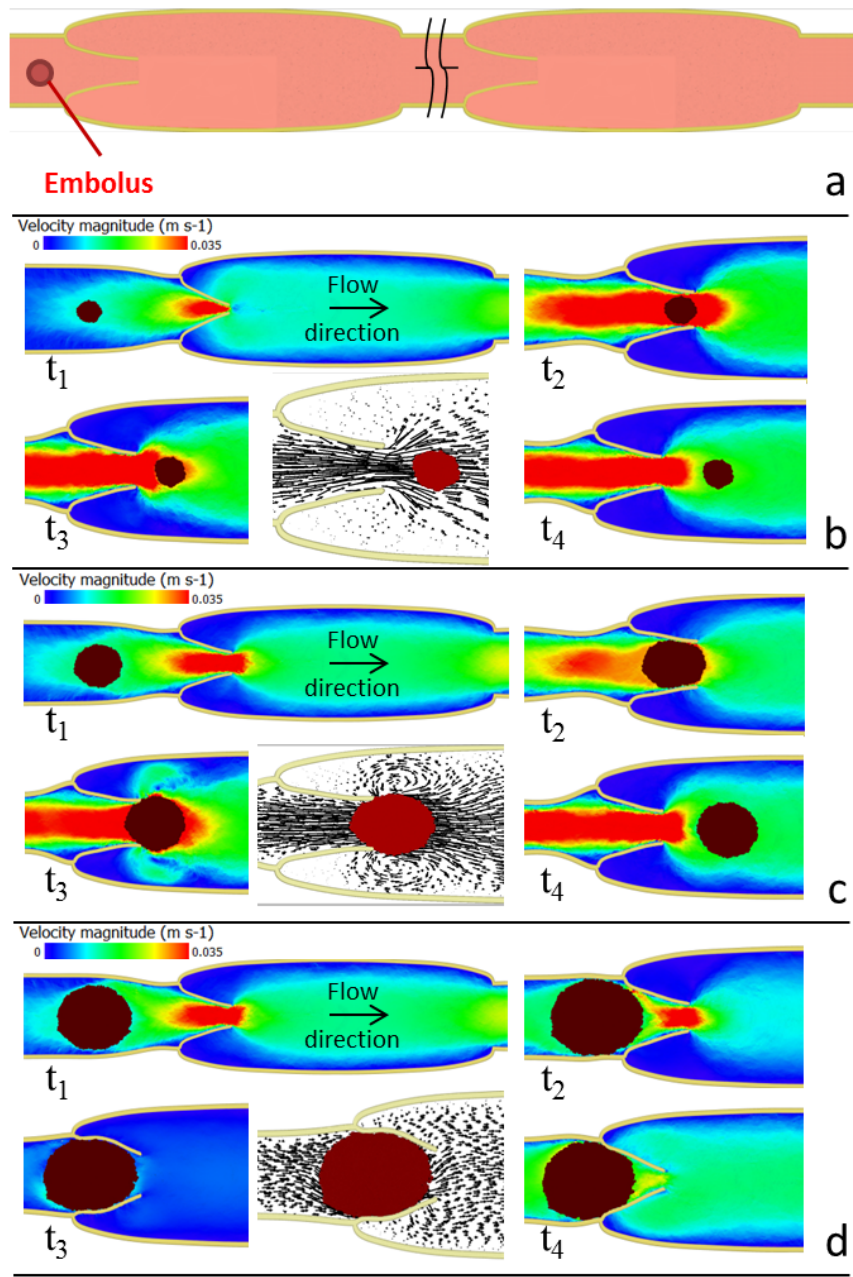
165 As mentioned, three parameters are investigated in this case: size, length and flexibility of the
 166 aggregate (Table 2).

167 3.2. Embolus displacement in the opening region

168 Initially, three circular emboli with diameters of $2.6 \cdot 10^{-3}$ m (Case D26 in Table 2), $5.2 \cdot 10^{-3}$ m
 169 (D52) and $7.8 \cdot 10^{-3}$ m (D78) are introduced into the flow (Fig. 3a). In the first case (Fig. 3b),
 170 the embolus is too small for impacting the flow and crosses the valve with no contact with the
 171 leaflets. No significant difference with the pure fluid case is observed.

172 In the second case (Fig. 3c), although the embolus diameter is bigger than the valve opening,
173 it can cross the valve because of its flexibility and the deformation of the leaflets. The
174 embolus is elastic [15] and recovers its initial shape after the valve. However, contrary to the
175 first case, the flow surrounding the embolus is considerably affected by the presence of the
176 embolus and two vortexes form around the valve.

177 In the third case (Fig. 3d), the embolus is bigger than the inlet valve chamber and despite the
178 large deformation of both the embolus and the valve, the embolus cannot cross the valve.



179

180 Fig. 3. Embolus position and velocity vectors at different times: a) $t = 0$ s for all emboli, b)

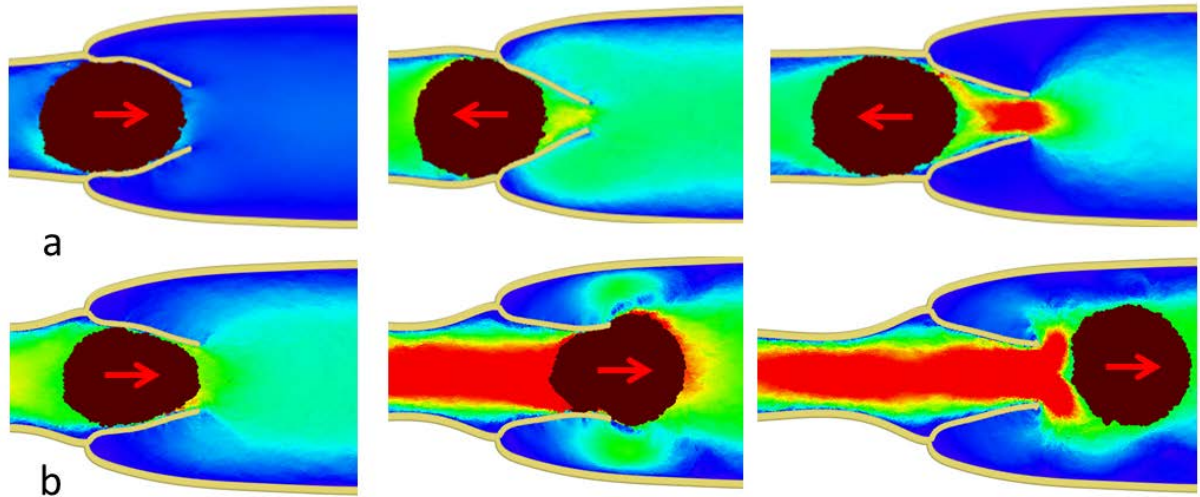
181 embolus D26, c) embolus D52, and d) embolus D78.

182 In reality, the embolus obstruction observed in Fig. 3d would probably resolve itself after a

183 certain time since, normally, the level of physical activity of an individual changes during the

184 day [28], while in our simulation we only considered low physical activity. In our

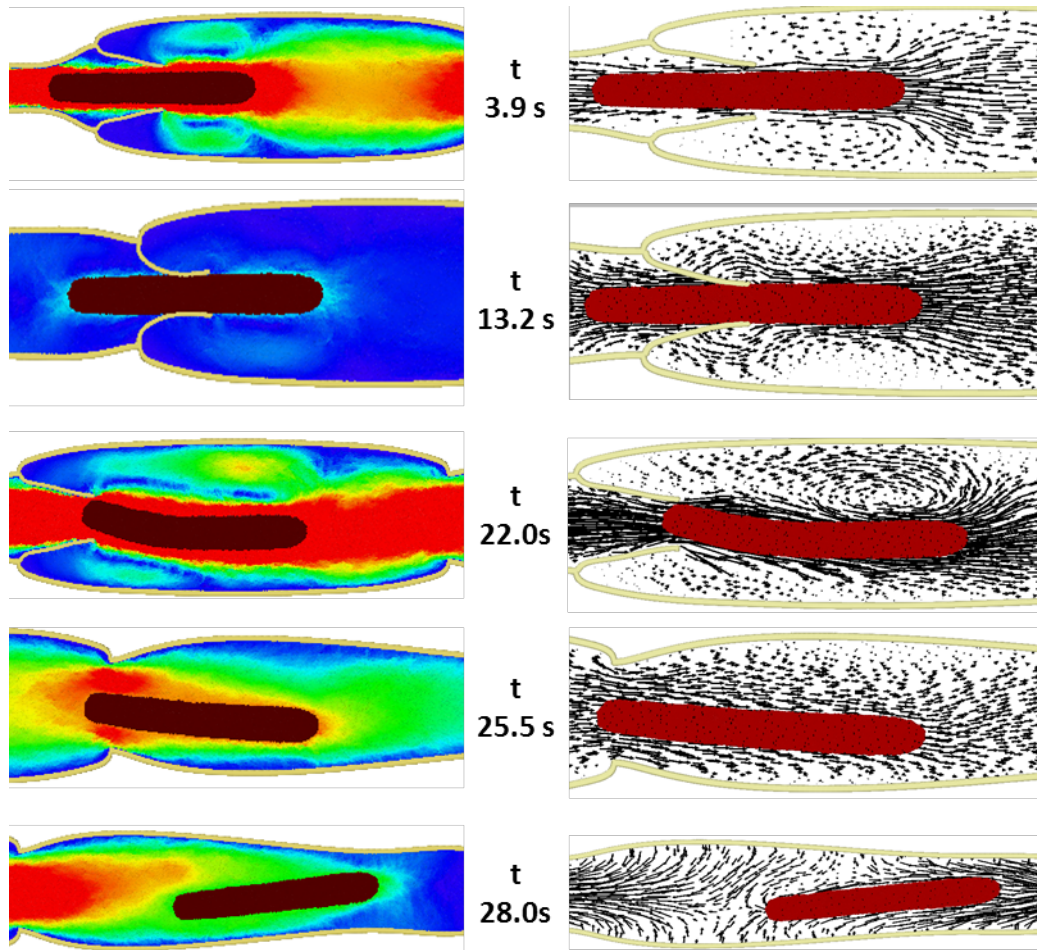
185 simulations, a similar situation (i.e. an embolus, initially stuck, crosses the valve after several
186 cycles) occurs when the flexibility of the embolus is higher (Fig. 4).



187

188 Fig. 4. Embolus of diameter $7.8 \cdot 10^{-3}$ m with different elasticity: a) $kb = 1 \cdot 10^4 \text{ J m}^{-2}$ (D78) and
189 b) $kb = 1 \cdot 10^3 \text{ J m}^{-2}$ (F103).

190 The vortexes observed in Fig. 3c and Fig. 4 are larger if the length of the embolus is longer as
191 in Fig. 5. In this case, both the flow and the valve behaviour are considerably altered by the
192 presence of the ‘sausage-like’ embolus.



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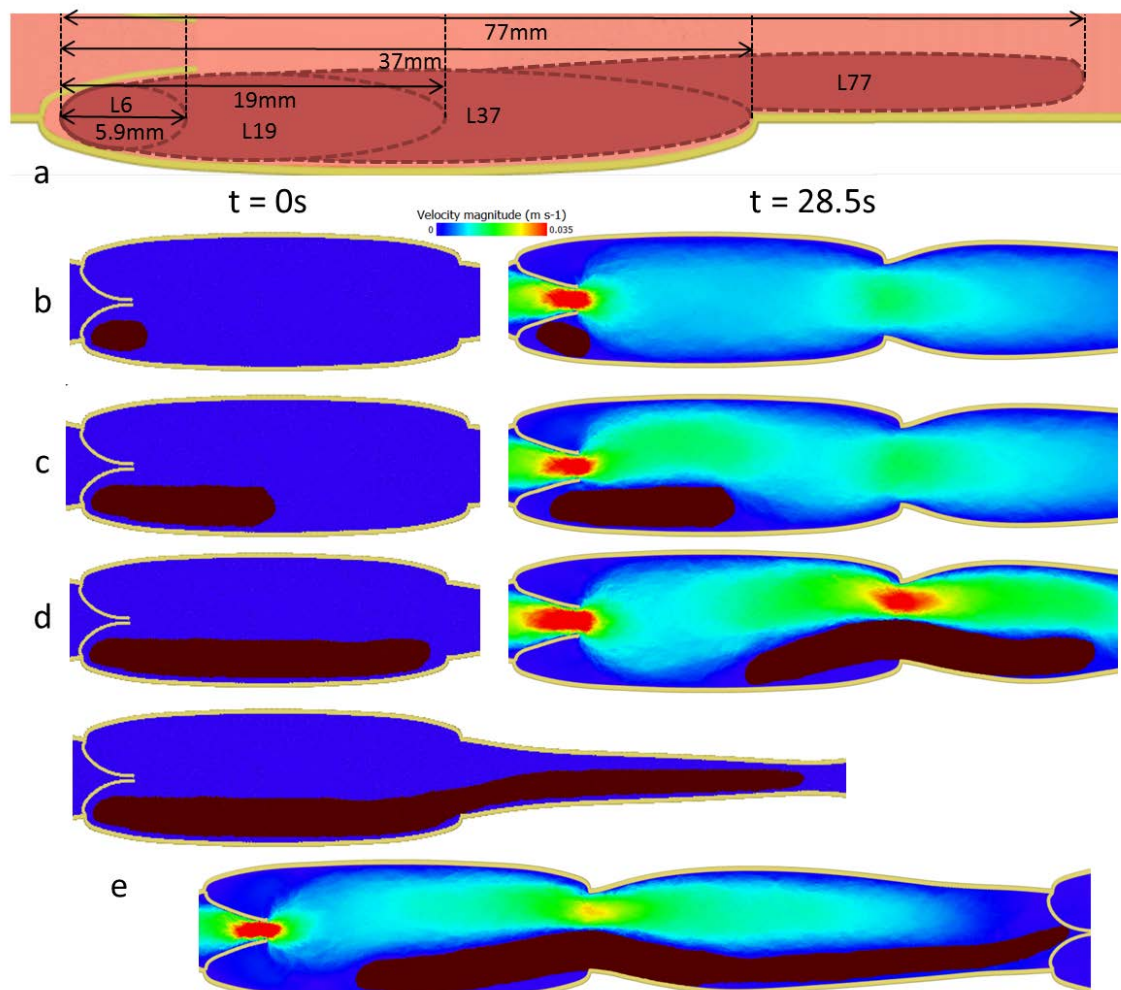
194 Fig. 5. Velocity magnitude and vectors of the flow and circulation of the embolus (L21) at
 195 different times.

196 3.3. Embolus displacement in the sinus region

197 In this section, an embolus is located behind Valve 1 (sinus region in Fig. 1). In the medical
 198 literature, it is not completely clear where emboli form, but they are often found in the sinus
 199 region. After they reach a certain size, they leave the sinus region, and move in the
 200 cardiovascular system. In this section, we show how the length of the embolus can affect its
 201 permanence in the sinus region. Four emboli with different lengths are simulated (Table 2):

202 5.9 mm (L6 in Table 2), 19 mm (L19), 37 mm (L37) and 77 mm (L77) and located in the
203 sinus region (Fig. 6a).

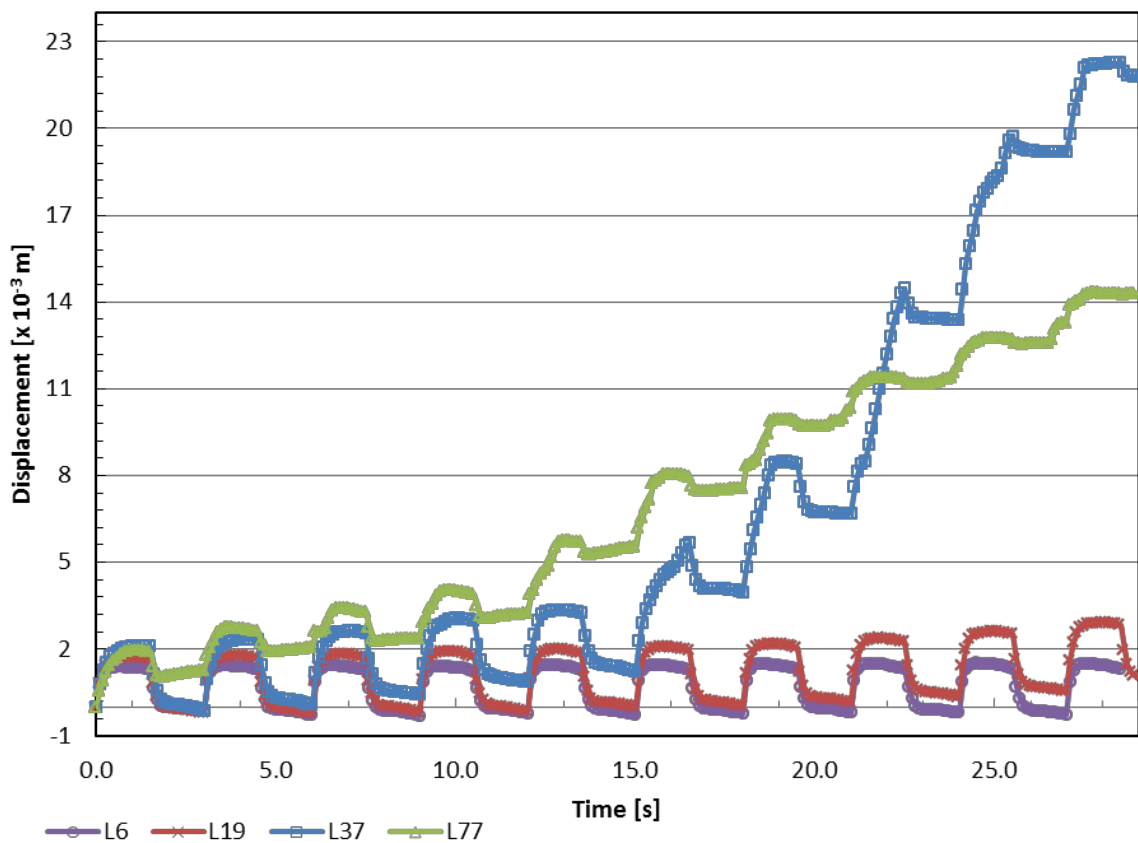
204 Fig. 6b and Fig. 6c show no significant displacement of embolus L6 and embolus L19 after 10
205 cycles while embolus L37 (Fig. 6d) and L77 (Fig. 6e) show a high displacement. In fact, each
206 embolus interacts with the fluid in a different way. The longer the embolus, the higher the
207 drag force that the liquid exchange with the embolus. This force, however, is not simply
208 proportional to its length, but it also depends on the local velocity at the location of the
209 embolus.



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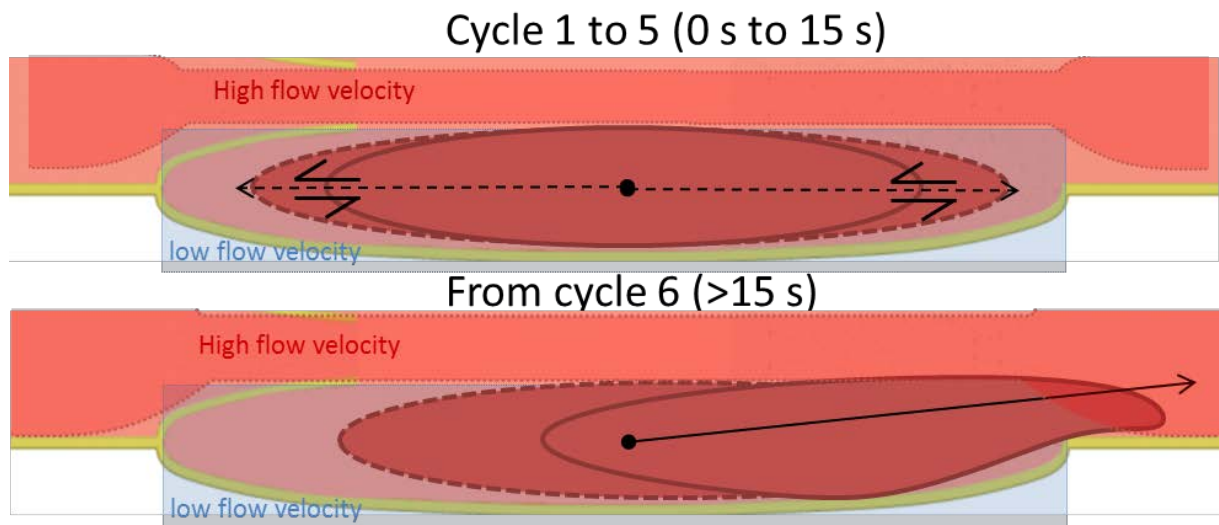
211 Fig. 6. Embolus position at t = 0 s and t = 28.5 s for a) L6, b) L19, c) L37, d) L77.

212 In Fig. 7, embolus displacement versus the simulation time indicates that the displacement
213 values oscillate every cycle (forward and backward embolus motion). Embolus L6 never
214 moves and only spins around itself (Fig. 6b) due to its “circular” shape. While embolus L19
215 begins to move slowly after 20 s. In both cases, the emboli remain in the low flow area (Fig.
216 8) where the flow velocities are the lowest. On the other extreme, embolus L77 continually
217 moves because the most of the embolus is located in the main flow area (Fig. 8). The
218 displacement of L37 is initially smaller than L77, because a lower fraction is in contact with
219 the high velocity area. However, once it is dragged away from the left end of the sinus it is
220 more easily captured by the main flow due to its smaller size.



221

222 Fig. 7. Time evolution of the local displacement for embolus L6, L19, L37, and L77.



223

224 Fig. 8. Schematic of embolus L37 movement in low flow region and high flow region before
 225 and after 15s.

226 4. Conclusions

227 Free emboli circulation in a valve environment has been studied using the Discrete Multi-
 228 Physics approach. We modelled both fluid and emboli dynamics as well as the leaflets
 229 deformation. In our previous studies [14, 17], an inlet fluid velocity was used to ensure the
 230 blood motion within the rigid channel, while here, the flow is governed by muscle
 231 contractions.

232 The results show that emboli with a size bigger than the valve can still cross the valve if they
 233 are flexible enough. This observation can be linked with the age of emboli in the body since
 234 the elasticity of an embolus depends on its life-time in the blood system [29], and the older
 235 the embolus the lower its flexibility.

236 The embolus length plays also a paramount role. In the main flow (opening region), the
 237 embolus can potentially generate new vortex area that can further favour platelets

238 aggregation. In the low flow (sinus region), the length of the embolus determines how long it
239 takes for the embolus to detach from the sinus region and move within the main flow.

240 The main conclusion of this work is that the presence of an embolus strongly affects the
241 dynamics of both the fluid and the leaflets in venous valves. Therefore, computer simulations
242 designed to support fundamental research in DVT should account for emboli if they aim at a
243 more realistic description of reality.

244 **Supporting Information**

245 Appendix A

246

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