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DOI:

[10.1016/j.compfluid.2018.01.037](https://doi.org/10.1016/j.compfluid.2018.01.037)

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*Document Version*

Peer reviewed version

*Citation for published version (Harvard):*

Ariane, M, Vigolo, D, Brill, A, Nash, FGB, Barigou, M & Alexiadis, A 2018, 'Using Discrete Multi-Physics for studying the dynamics of emboli in flexible venous valves', *Computers and Fluids*, vol. 166, pp. 57-63.  
<https://doi.org/10.1016/j.compfluid.2018.01.037>

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Checked for eligibility: 21/03/2018  
<https://doi.org/10.1016/j.compfluid.2018.01.037>

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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].

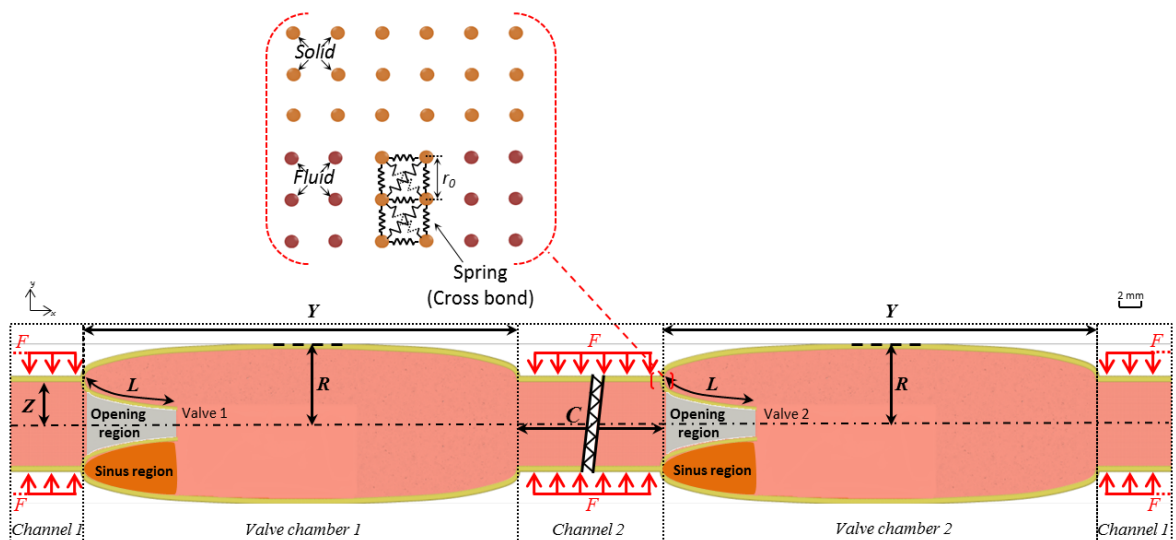
55 In this approach, the liquid is represented by SPH particles that interact with each other by  
56 viscous and pressure forces and the tissues by MSM particles inter-connected by means of  
57 computational springs (to model the elastic modulus) and dashpots (to model viscoelasticity).  
58 The essential 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).



83

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

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

### 97 **2.3. Model parameters**

98 In our simulations, the geometry is divided into 168676 particles spaced of  $10^{-4}$  m: 584 for the  
99 valves, 10722 for the walls, and 157370 for the fluid area. As mentioned, SPH particles are  
100 used for the fluid, stationary (solid) particles for the valve chamber walls and MSM particles  
101 for the flexible walls and the leaflets. Three layers of particles are used for the walls and two  
102 for each leaflet, with thicknesses of  $3 \cdot 10^{-4}$  m and  $2 \cdot 10^{-4}$  m, respectively. The flow is laminar  
103 [13, 25, 26] and blood is here considered a Newtonian fluid [15, 27]. Table 1 gathers all the  
104 parameters used in the simulation.

105

106

107

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 $\Delta r$	$1 \cdot 10^{-4}$ m
Smoothing length $h$	$2.5 \cdot 10^{-4}$ m
Artificial sound speed $c_0$	$10$ m s <sup>-1</sup>
Density $\rho_0$	$1056$ kg m <sup>-3</sup>
Viscosity $\mu_0$	$0.0035$ Pa s
Time step $\Delta t$	$10^{-6}$ s
Force $F$	$0.008$ N
MSM (Eqs. A.10)	
Parameter	Value
Hookian coefficient $k_b$ (Wall)	$1 \cdot 10^5$ J m <sup>-2</sup>
Hookian coefficient $k_b$ (membrane)	$5 \cdot 10^6$ J m <sup>-2</sup>
Viscous damping coefficient $k_v$ (Wall)	$1$ kg s <sup>-1</sup>
Viscous damping coefficient $k_v$ (membrane)	$0.1$ kg s <sup>-1</sup>
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).

134

135

136

137

Table 2. Simulation parameters used for the embolus aggregate.

<b>Variation of the diameter of the embolus (spherical) with <math>k_b = 1 \cdot 10^4 \text{ J m}^{-2}</math></b>		
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
<b>Variation of the length of the embolus with height = <math>2.6 \cdot 10^{-3} \text{ m}</math> and <math>k_b = 1 \cdot 10^4 \text{ J m}^{-2}</math></b>		
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
<b>Variation of the flexibility of the embolus (spherical) with diameter = <math>7.8 \cdot 10^{-3} \text{ m}</math></b>		
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

138

### 3. Results and discussion

139

#### 3.1. Hydrodynamics

140

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

141

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

142

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

143

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

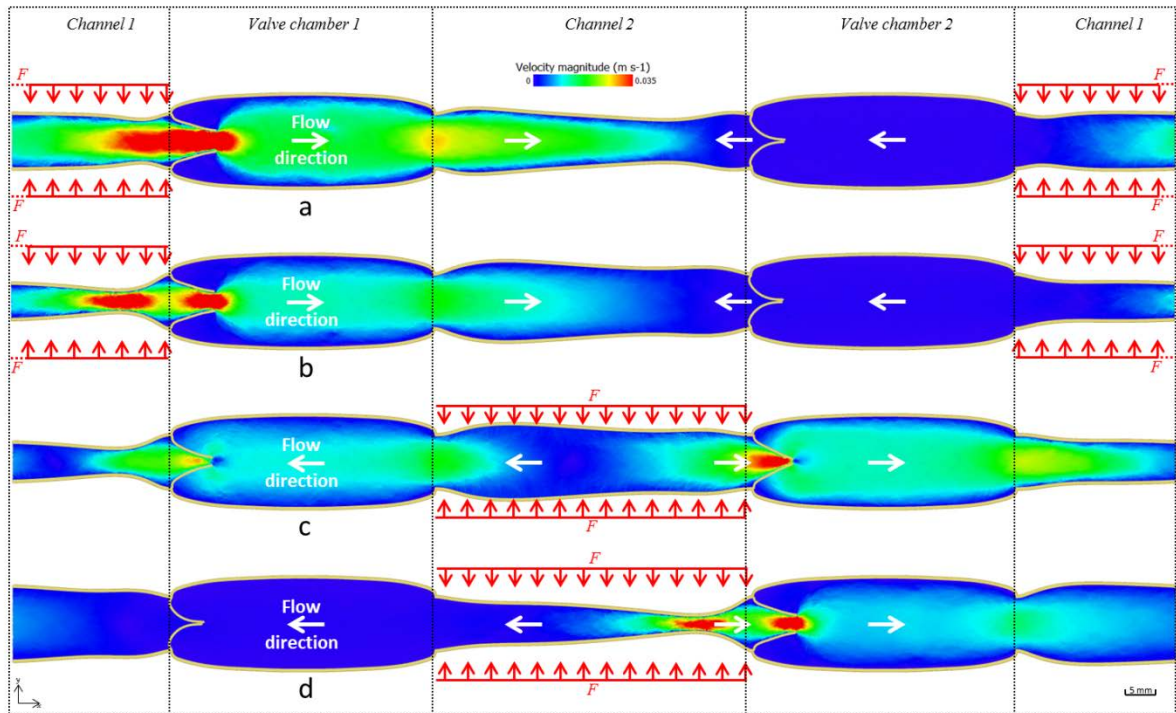
144

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  $0.035 \text{ m s}^{-1}$  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.

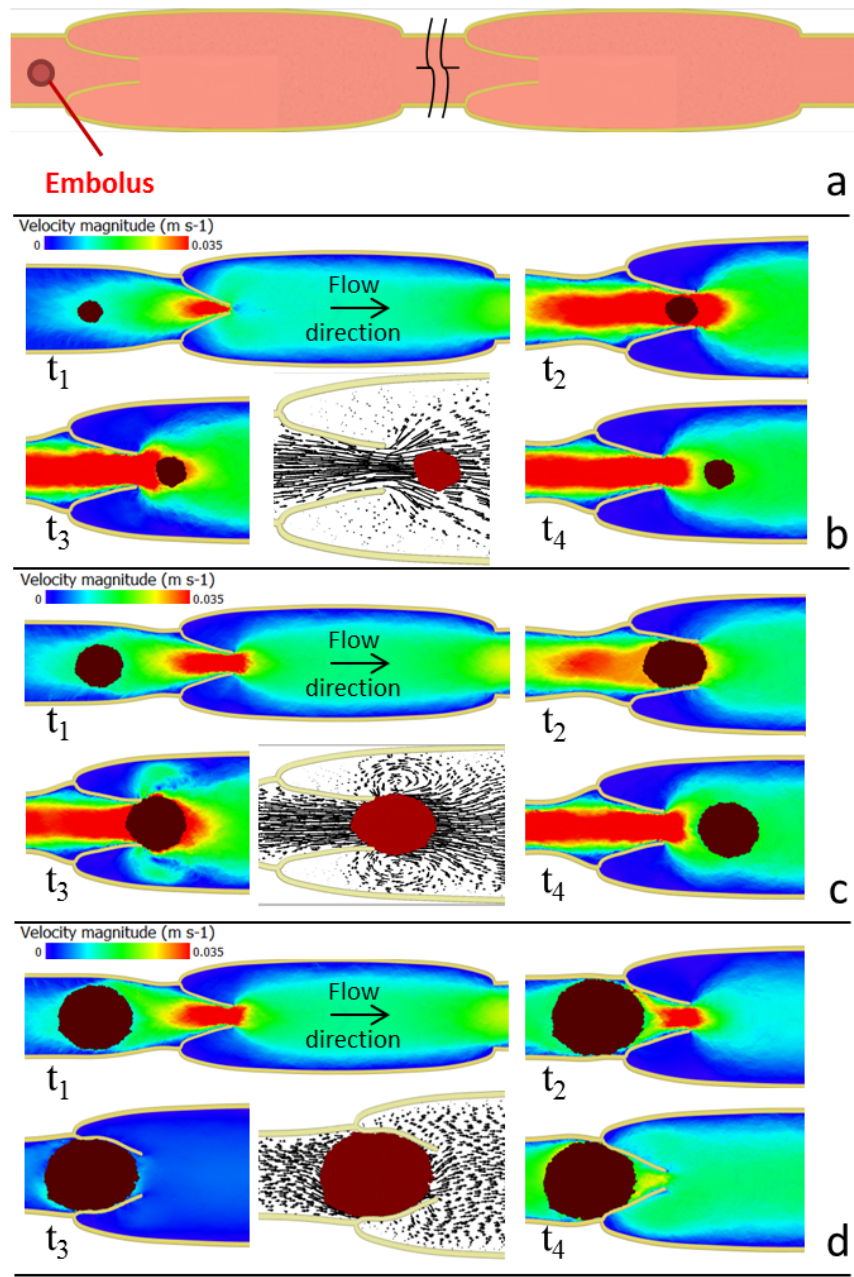
165 As mentioned, three parameters are investigated in this case: size, length and flexibility of the  
 166 aggregate (Table 2).

### 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)

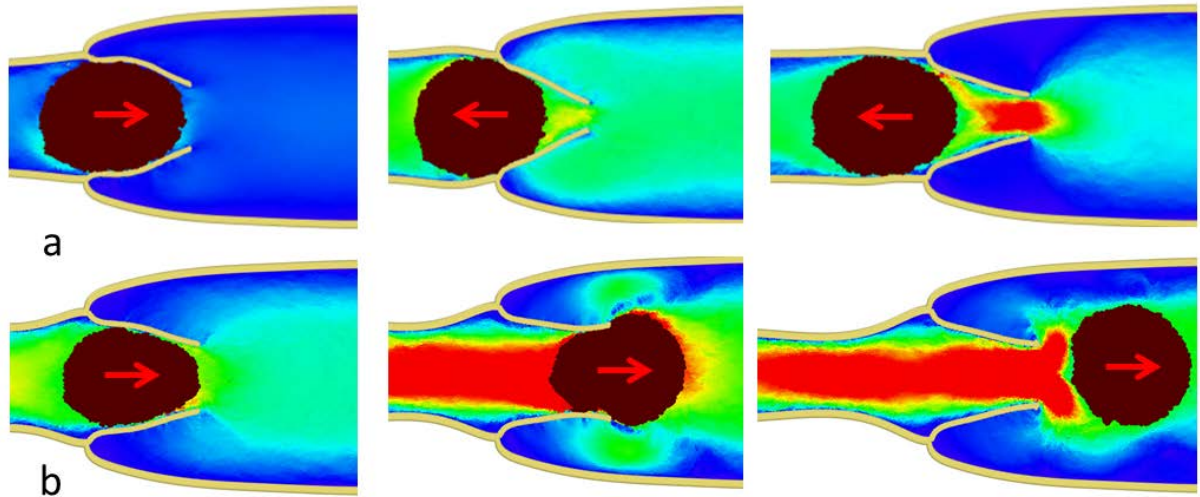
181 embolus D26, c) embolus D52, and d) embolus D78.

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).

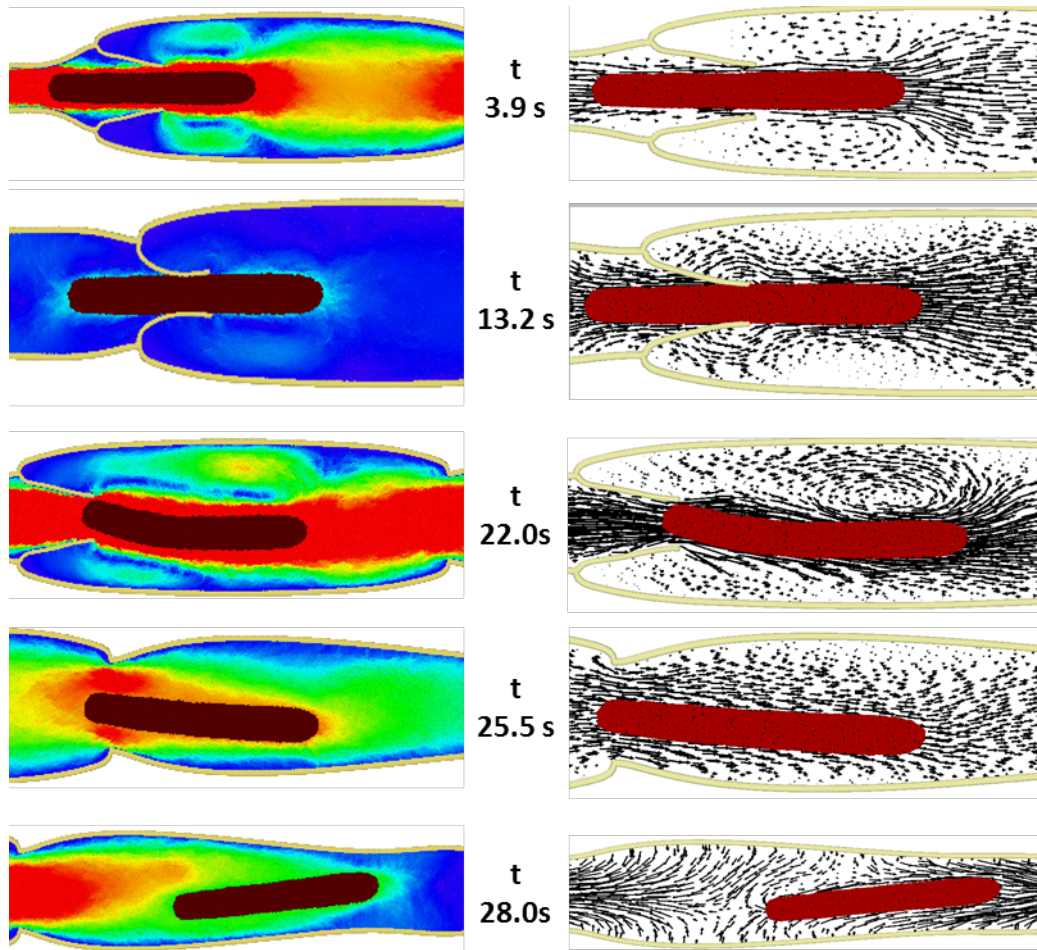


187

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.





193

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

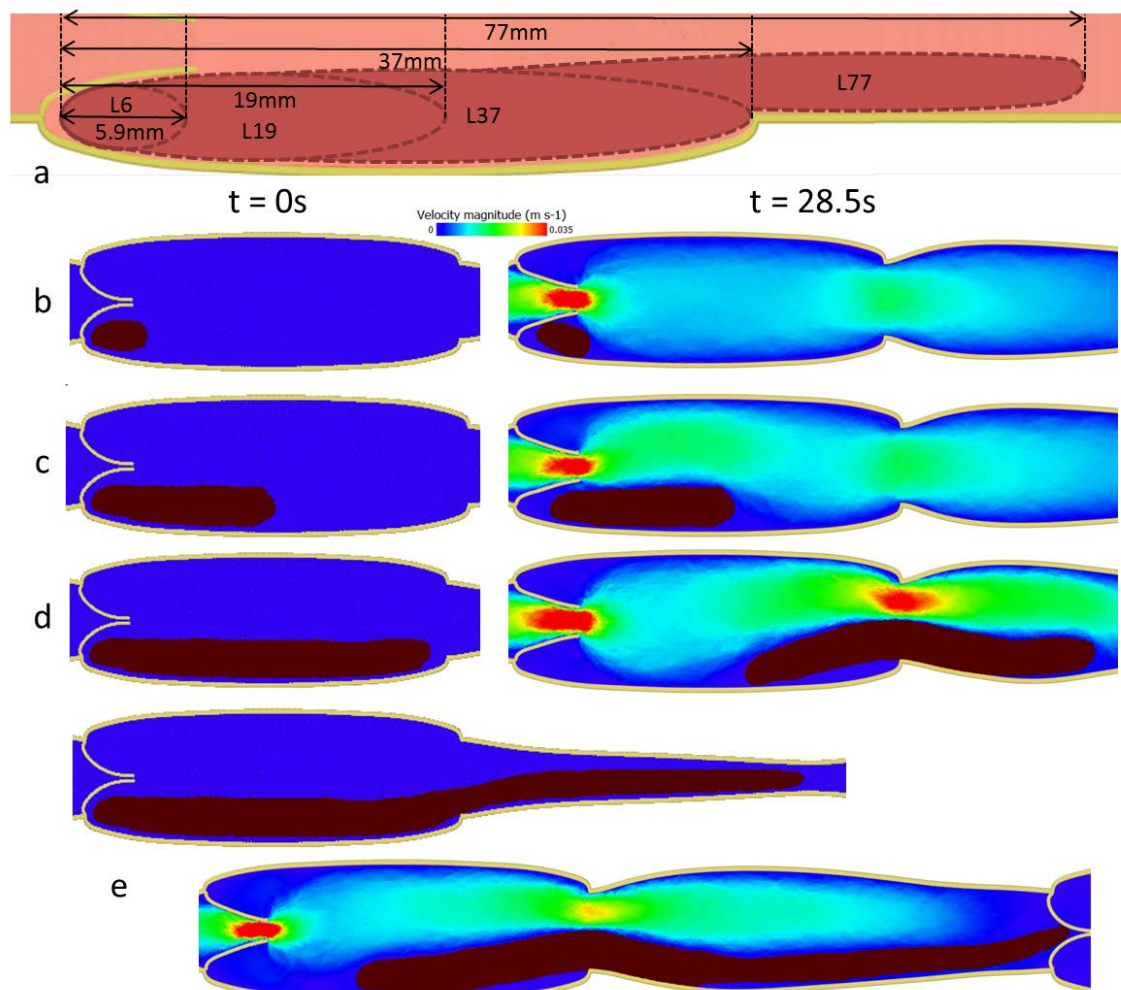
### 196 3.3. Embolus displacement in the sinus region

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).

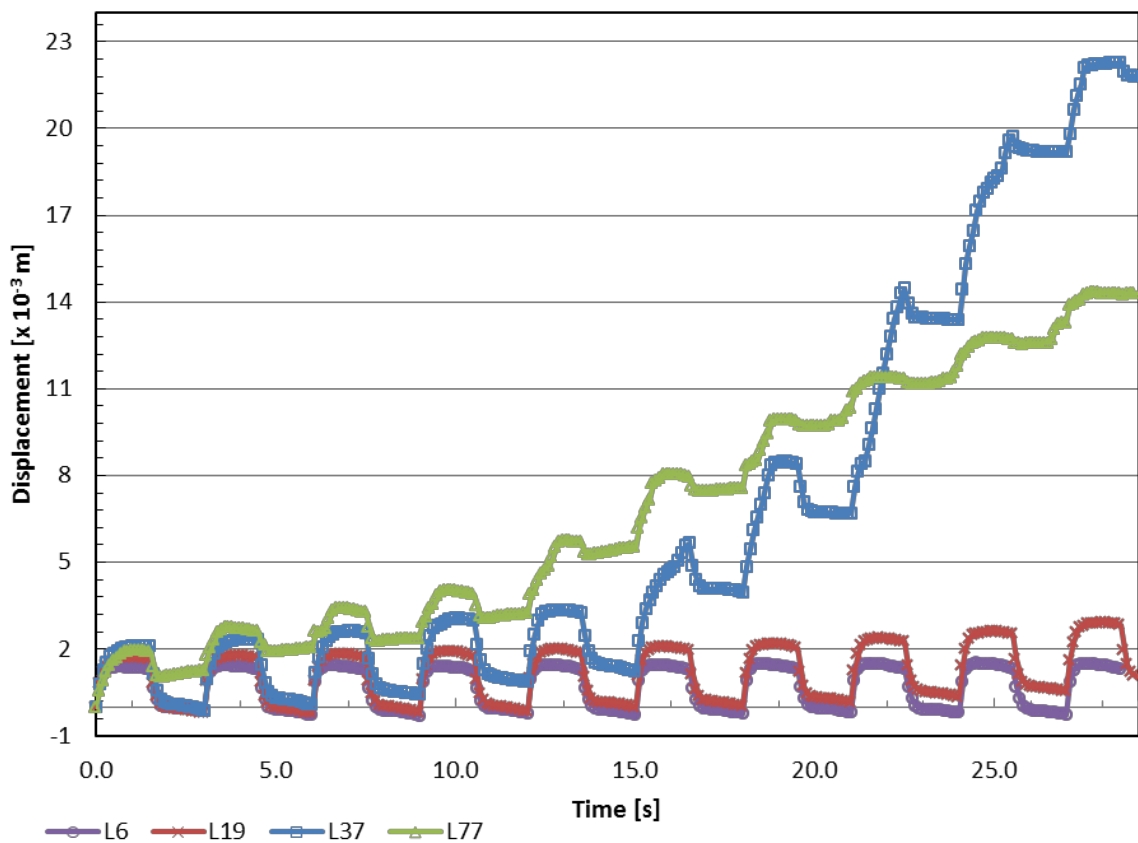
204 Fig. 6b and Fig. 6c show no significant displacement of embolus L6 and embolus L19 after 10  
205 cycles while embolus L37 (Fig. 6d) and L77 (Fig. 6e) show a high displacement. In fact, each  
206 embolus interacts with the fluid in a different way. The longer the embolus, the higher the  
207 drag 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.



210

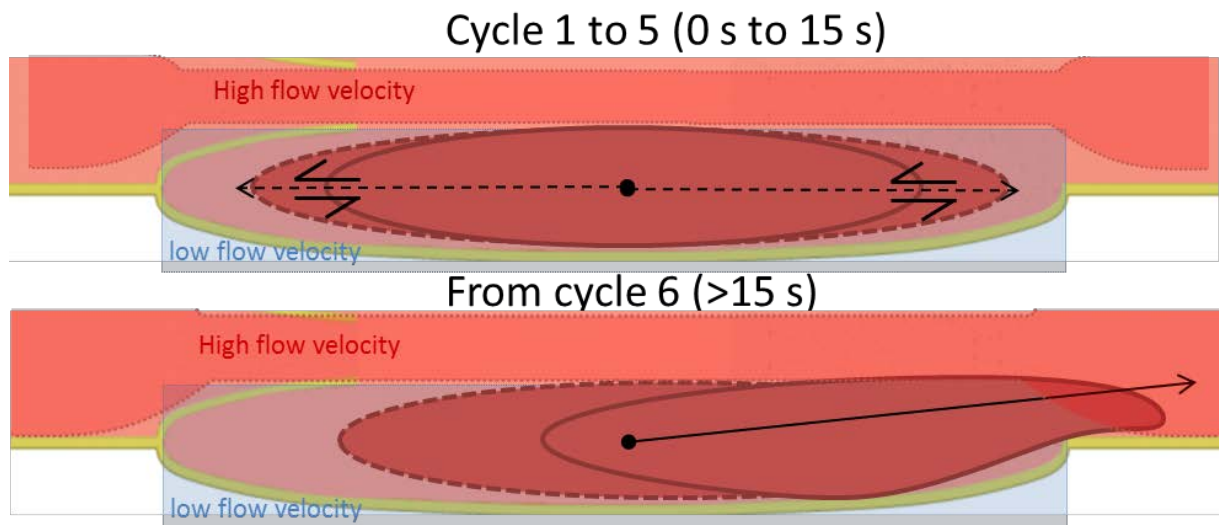
211 Fig. 6. Embolus position at t = 0 s and t = 28.5 s for a) L6, b) L19, c) L37, d) L77.

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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