18th Brazilian Congress of Thermal Sciences and Engineering
November 16-20, 2020 (Online)

ENC-2020-0584
COMPARATIVE STUDY BETWEEN EULERIAN AND LAGRANGIAN APPROACHES FOR THE ANALYSIS OF HEMOLYTIC AND PLATELET LYSIS INDEX WITH COUETTE FLOW

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Abstract. *The applications of clinical cardiac assistance systems, when in contact with the bloodstream, modify the flow in its insertion region. These changes can trigger harmful processes like hemolysis and thrombosis. The hemodynamic effects are related to shear stress and exposure time acting on blood cells. Computational fluid dynamics has been widely applied to understand the mechanics of fluids behind blood damage through two approaches: Eulerian and Lagrangian. The Eulerian approach has raised doubts in academic community due to some inherent limitations of such methodology. On the other hand, studies based on the Lagrangian approach have developed different methodologies in an attempt to better understand the mechanism of hemolysis and thrombus formation due to the contact of clinical instruments with blood. In order to compare these methods, this work reproduces the Couette flow for analysis of hemolytic and platelet lysis index. The reproduced experiment consists of a numerical simulation of blood flow in laminar regime. The results were compared with experimental data from the literature, and both methods showed proximity for a simple flow.*

Keywords: *Couette flow, Hemolysis, Thrombosis, Eulerian Approach, Lagrangian Approach*

1. INTRODUCTION

The applications of cardiac assistance systems, widely used in clinical procedures, present some adversities. When in contact with bloodstream, clinical devices and endoprostheses significantly modify the flow pattern. Therefore, these changes can trigger harmful processes in blood, such as hemolysis and thrombosis. The hemodynamic effects due to endoprostheses implants for aneurysms in the aorta, cause a major change in the shear stress field due to non-physiological conditions of the flow (Tillman et al., 1984). The use of central venous access catheters for hemodialysis can generate regions of blood stagnation and areas with high shear that induce platelet activation and cause damage to red blood cells (Mareels et al., 2007). These effects were also studied by Haniel et al. (2019) and Consolo et al. (2017). The use of ventricular assist devices (VAD) for patients with heart failure (HF) is another example, which can induce damage to blood components, since it inevitably generates non-physiological shear stresses (Zengsheng et al., 2019, and Tchantchaleishvili et al., 2014).

With the advent of computational fluid dynamics (CFD), the model proposed by Giersiepen et al. (1990) has been adopted in an attempt to understand, from the point of view of fluid mechanics, how hemodynamic processes are triggered. The model was incorporated as transport equations, which allows the Eulerian and Lagrangian analysis of the process. This tool has wide applicability, present in several cardiovascular studies, such as the analysis in central venous catheters (Mareels el al., 2007) and the investigation of stenosed arterial models (Zhou et al., 2018). Considering that, the objective of the present study was to compare the Eulerian and Lagrangian approaches in order to investigate the use of both in numerical simulations of blood flow through medical devices.

The Lagrangian approach uses a finite set of particles to discretize the domain, where each particle represents a fluid element followed over time in its trajectory. In this analysis, the damage index is integrated along flow pathlines, which allows to model the damage history suffered by the cells. Five models based on the Lagrangian methodology were proposed in an attempt to establish the most appropriate approach for the study of hemodynamic effects in cardiac assist devices (Taskin et al., 2012).

On the other hand, the Eulerian approach widely used in CFD analysis starts from the assumption of observing a fixed field in space. In this method, the blood damage index is integrated in the control volume domain. However, the Eulerian approach has raised doubts in academic community due to some inherent limitations of such methodology. It is known that the power-law for the calculation of hemodynamic effects has characteristics of Lagrangian approach, and its conversion from Lagrangian to Eulerian may cause implications. According to Faghih and Sharp (2019), there are two main limitations to this remodeling. The former arises during this transformation, as the spatial dependence of the exposure time to shear stress is neglected. Thus, variations between exposure time and flow time, average velocity, local velocity and shear stress along the streamlines are ignored. This suggest that the Eulerian approach could be only suitable for analysis of steady, uniaxial flows with constant velocity along the streamlines. Another limitation is related to the linearization process, since the distribution of an exponent through an integral is restricted by a unitary exponent or a constant function throughout the regime, which does not include hemodynamic effects. Therefore, these limitations require a correction to Eulerian analysis, which is difficult for complex flows of cardiovascular devices.

It is known that the main causes of hemolysis and thrombus formation are related to the shear stress, which blood cells are exposed, as well as the time of exposure to that stress. According to Goubergrits and Affeld (2004), hemolysis is dependent on cell age and history of sublethal damage, caused by limiting shear stress and exposure time. In addition, the time and level of shear exposed by blood cells can cause platelet activation or lysis, which is related to the platelet lysis index (PLI), (Haniel et al., 2019, and Goubergrits and Affeld, 2004). To describe the dependence on shear stress and time of exposure to the hemolysis process, Giersepen et al. (1990) proposed a mathematical model applied to *in vitro* investigations of 25 different aortic valve prostheses. The experiments were carried out under the conditions of the classical Couette flow, using a methodology proposed by Heuser and Opitz (1980). As a result, the first power-law model for the hemolytic index (HI) was developed as a function of shear stress (< 255 Pa) and time exposition (< 0.7 s).

In this context, the work proposed here reproduces the Couette flow for the analysis of hemolytic and platelet lysis index. The reproduced experiment consists of a numerical simulation of laminar and Newtonian blood flow. For shear stress calculations, its proportionality relationship with the fluid strain rate was used, where the dynamic viscosity was the proportionality constant. Through computational fluid dynamics (CFD), shear stress and exposure time values originated from the experiment by Giersiepen et al. (1990) were used for the analysis of hemodynamic effects. Therefore, the mathematical models from the Eulerian and the Lagrangian perspectives were used to compare the computational model with the experimental data from literature.

2. MATERIALS AND METHODS

2.1 Geometry Model

The numerical simulations of the Couette experiment (Giersiepen et al., 1990) were based on a two-dimensional rectangular model, as shown in Fig. 1. ANSYS-Fluent® 20.1 (ANSYS Inc., Lebanon, NH, USA) software was used for spatial discretization and solution of Navier-Stokes equations. The transport equations for the hemolytic index and the thrombogenic potential of Eulerian approach were implemented using User-defined function (UDF), which are based on C language.

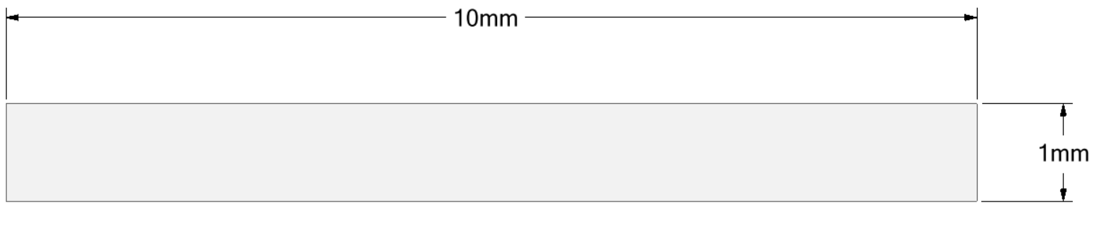

Figure 1. 2-D domain of the fluid in a Couette flow.

2.2 Mesh Convergence Test

The development of a finite volume mesh was carried out through the grid convergence test based on the ASME V&V 20-2009 standard. The refinement factor r was close to 1.3, and the maximum relative error between the properties of the Hemolytic Index (HI) and the Platelet Lysis Index (PLI), through the power-law method, was defined less or equal to 1%. This step indicates that the properties of interest no longer depend on the elements size, h.

The meshes were developed from first-order quadrilateral elements, with a refinement of seven layers near the wall. Their quality was measured using a value that assesses skewness of elements, ranging from 0 to 1. This measure was targeted at less than 0.25, considering that the closer to 0 the closer element gets to a quadrilateral with 90^{o}. To evaluate the meshes, simulations were performed for four shear stresses, whose values: 57 Pa, 108 Pa, 170 Pa and 255 Pa. For each one of the shear stresses, the values of HI and PLI of four points along the geometry were analyzed.

Table 1 shows the characteristics and progression of the refinement developed from four meshes for each one of the four shear stresses. The relative error described in the table shows the maximum percentage value among those found. Once we reached a small enough error value between meshes 4 and 3, mesh 3 with 136653 elements and 137888 nodes was chosen.

Table 1. Mesh convergence test.

	Mesh 1	Mesh 2	Mesh 3	Mesh 4
# Elements	46875	78850	136653	227205
# Nodes	47576	79776	137888	228793
Relative Error	5.23	3.21	0.33	-
h	4.62E-05	3.56E-05	2.71E-05	2.10E-05
r	-	1.30	1.32	1.29

2.3 Fluid Rheology and Boundary Conditions

Blood was considered Newtonian with viscosity μ = 0.0035 Pa.s and density ρ = 1060 kg/m³ (Marom and Bluestein, 2015).

In the Couette flow, a plate with constant velocity u moves parallel to another stationary plate with the no slip condition. In this context, the flow presents a linear velocity profile. A notable aspect of this flow is that the shear stress is constant. Thus, the shear stress of an element at a height normal to the y-plates is defined by the dynamic viscosity μ, and the shear rate $\partial u/\partial y$, as follows:

$$\tau(y) = \mu \cdot \frac{\partial u}{\partial y} \tag{1}$$

The simulated shear stresses (57 Pa, 108 Pa, 170 Pa and 255 Pa) and exposure times (0.007 s, 0.0027 s, 0.113 s and 0.7 s) were presented in the experiment by Giersiepen et al. (1990), in order to compare their mathematical model with the results obtained by the Eulerian and Lagrangian approaches.

Coupled algorithm was used for velocity-pressure coupling. For gradients and pressure discretization, the Least Squares Cell Based and the Second Order algorithms were adopted, respectively. In addition, momentum and user scalars (Residence Time, Hemolytic Index and Platelet Lysis Index) were discretized by the first order Upwind. As a convergence condition, a value of 10^{-6} was applied to the residuals for all calculations.

2.4 Numerical Models of Hemolytic Index (HI) and Platelet Lysis Index (PLI)

The numerical models used to estimate the hemodynamic effects of hemolysis and thrombosis were proposed by Giersiepen et al. (1990), from experiments in which blood cells were exposed to shear stresses (< 255 Pa), during a certain exposure time (< 0.7 s). The values of the constants for power-law (Eq. 2) were determined by regressing the data obtained experimentally.

$$X = C \cdot t^{\alpha} \cdot \tau^{\beta} \tag{2}$$

where, τ is shear stress, and t_{exp} is exposure time.

For hemoglobin (Hb) release by red blood cells:

$$HI(\%) = \frac{\Delta Hb}{Hb} \times 100 = 3.62\ 10^{-5}\ t_{exp}^{0.785}\ \tau^{2.416} \tag{3}$$

For cytoplasm enzyme (LDH) release by platelets:

$$PLI(\%) = \frac{\Delta LDH}{LDH} \times 100 = 3.31\ 10^{-6}\ t_{exp}^{0.77}\ \tau^{3.075} \tag{4}$$

2.4.1 Eulerian Approach

According to Taskin et al. (2012), the scalar transport equation for hemolysis, considering the Eulerian approach, is expressed as:

$$\frac{d(\Delta Hb')}{dt} + v\rho \cdot \nabla\left(\Delta Hb'\right) = S \tag{5}$$

where,

$$\Delta Hb' = \Delta Hb^{1/\alpha} \tag{6}$$

and S is the source term defined as:

$$S = \rho\ (Hb \cdot C \cdot \tau^{\beta})^{1/\alpha} \tag{7}$$

2.4.2 Lagrangian Approach

For the analysis of the Lagrangian approach, 122 particles were sown in the Couette flow. The five mathematical models exposed in the Taskin et al. (2012) study were used for this analysis. The first one was used by several researchers, such as Chan et al. (2002), Yano et al. (2003) and Song et al. (2004). The mathematical equation considers blood damage as the average of the streamlines in the output integrated for each time interval, starting from the power-law, as shown in Eq. 8:

$$HI1 = \int_{inlet}^{outlet} C \cdot dt_{exp}^{\alpha} \cdot \tau^{\beta} = \sum_{inlet}^{outlet} C \cdot \Delta t_{exp}^{\alpha} \cdot \tau^{\beta} \tag{8}$$

The second one calculates accumulated damage by integrating the time derivative of the power-law method. This model (Eq. 9) was adopted in the studies by Zimmer et al. (2000), Lim et al. (2001) and Grigioni et al. (2002).

$$HI2 = \sum_{inlet}^{outlet} \alpha \cdot C \cdot t_{exp}^{\alpha-1} \cdot \tau^{\beta} \cdot \Delta t_{exp} \tag{9}$$

Garon and Farinas (2004) developed the third one (Eq. 10), based on the sum of this linearized damage, as:

$$HI3 = C \left(\sum_{inlet}^{outlet} \Delta t\ \tau^{\beta/\alpha} \right)^{\alpha} \tag{10}$$

Subsequently, the fourth one was developed by Grigioni et al. (2005), encompassing the dose of physical mechanisms D, acting throughout the trajectory of the blood cell in the concept of the second method, as follows:

$$HI4 = \sum_{inlet}^{outlet} \alpha \cdot C \cdot \left[\sum_{j=1}^{i} \tau\left(t_j\right)^{\frac{\beta}{\alpha}} \cdot \Delta t_j + D\left(t_0\right) \right]^{\alpha-1} \cdot \tau(t_j)^{\beta/\alpha} \cdot \Delta t_i \tag{11}$$

where,

$$D = t_{exp} \cdot \tau^{\beta/\alpha} \tag{12}$$

Finally, the fifth one proposed by Goubergrits and Affeld (2004), like the previous one, considers the history of blood damage, based on the conjecture of the hemodynamic effect as a function of cell age and sublethal cell damage, so that the damage at a given point in time is independent of how the existing blood damage arose. Thus, it is defined as:

$$HI5\left(t+\Delta t\right) = C \cdot \left(t_{eff} + \Delta t\right)^{\alpha} \cdot \tau(t+\Delta t)^{\beta} \tag{13}$$

where, t_{eff} is:

$$t_{eff} = \left(\frac{HI5(t)}{C \cdot \tau(t+\Delta t)^{\beta}} \right)^{1/\alpha} \tag{14}$$

The methods for the hemolytic index represented above were extrapolated to the platelet lysis index, with the alteration of the constants (C, α and β) found by Giersiepen et al. (1990) for the power-law. It was investigated in this study whether extrapolation may be suitable to PLI.

3. RESULTS AND DISCUSSION

Table 2 shows the results for 16 points, resulting from the combination of four shear stresses and four exposure times for hemolytic index. Table 3 presents the same points for the platelet lysis index.

Table 2. Comparison between the Eulerian and Lagrangian approaches with experimental data for the HI.

τ (Pa)	t_{exp} (s)	HI Experimental	HI Eulerian	HI1 Lagrangian	HI2 Lagrangian	HI3 Lagrangian	HI4 Lagrangian	HI5 Lagrangian
57	0.007	0.0129	0.0130	0.0456	0.0125	0.0126	0.0125	0.0126
	0.027	0.0371	0.0373	0.1229	0.0361	0.0368	0.0361	0.0368
	0.113	0.1142	0.1162	0.3466	0.1123	0.1142	0.1123	0.1142
	0.7	0.4779	0.4849	1.7187	0.4839	0.4874	0.4838	0.4874
108	0.007	0.0602	0.0607	0.2079	0.0581	0.0589	0.0581	0.0589
	0.027	0.1738	0.1763	0.5450	0.1684	0.1716	0.1684	0.1716
	0.113	0.5347	0.5465	1.6309	0.5317	0.5390	0.5316	0.5390
	0.7	2.2380	2.2366	8.1149	2.2182	2.2310	2.2177	2.2310
170	0.007	0.1802	0.1802	0.6105	0.1754	0.1785	0.1754	0.1785
	0.027	0.5201	0.5283	1.5776	0.5092	0.5186	0.5091	0.5186
	0.113	1.6001	1.6346	5.0730	1.5900	1.6076	1.5897	1.6076
	0.7	6.6969	6.6951	23.5104	6.6506	6.6890	6.6491	6.6890
255	0.007	0.4801	0.4837	1.5763	0.4640	0.4723	0.4640	0.4723
	0.027	1.3853	1.4049	4.2823	1.3713	1.3932	1.3709	1.3932
	0.113	4.2616	4.3521	14.2868	4.3072	4.3460	4.3060	4.3460
	0.7	17.8366	17.8291	68.2421	17.7223	17.7952	17.7163	17.7952

Table 3. Comparison between the Eulerian and Lagrangian approaches with experimental values for the PLI.

τ (Pa)	t_{exp} (s)	PLI Experimental	PLI Eulerian	PLI1 Lagrangian	PLI2 Lagrangian	PLI3 Lagrangian	PLI4 Lagrangian	PLI5 Lagrangian
57	0.007	0.0182	0.0203	0.0707	0.0176	0.0179	0.0176	0.0179
	0.027	0.0514	0.0573	0.1862	0.0500	0.0510	0.0500	0.0510
	0.113	0.1549	0.1752	0.5114	0.1525	0.1554	0.1525	0.1554
	0.7	0.6308	0.7109	2.5021	0.6424	0.6475	0.6423	0.6475
108	0.007	0.1298	0.1448	0.4911	0.1253	0.1270	0.1253	0.1270
	0.027	0.3671	0.4130	1.2546	0.3558	0.3632	0.3558	0.3632
	0.113	1.1053	1.2564	3.6687	1.1022	1.1190	1.1019	1.1190
	0.7	4.5012	4.9742	17.8795	4.4577	4.4864	4.4563	4.4864
170	0.007	0.5238	0.5801	1.9415	0.5097	0.5195	0.5097	0.5195
	0.027	1.4812	1.6703	4.8859	1.4519	1.4813	1.4515	1.4813
	0.113	4.4599	5.0725	15.4060	4.4415	4.4958	4.4401	4.4958
	0.7	18.1628	20.0754	69.6585	18.0234	18.1396	18.0178	18.1396
255	0.007	1.8225	2.0348	6.5396	1.7616	1.7961	1.7614	1.7961
	0.027	5.1533	5.8076	17.3414	5.1099	5.1997	5.1080	5.1997
	0.113	15.5171	17.6317	57.0936	15.7706	15.9276	15.7645	15.9276
	0.7	63.1924	69.8382	265.6665	62.7373	63.0246	62.7078	63.0246

As noted, for HI the first Lagrangian model presented higher error in relation to the experiment by Giersepen et al. (1990), showing to be unsuitable for use in applications like this. The other methods were close to the experiment with errors less than 3.5%, especially the Eulerian approach and the third and fifth Lagrangian methods.

The same as for HI, the first Lagrangian model presented a greater discrepancy in relation to the experiment. Similar to the previous graph, the other Lagrangian methods showed a proximity with errors less than 3.5%. However, the Eulerian method presented higher error for PLI (maximum error of 13.74%) than for HI (maximum error of 2.2%).

Figures 2 and 3 illustrate the contours of HI and PLI, respectively, in the streamlines in the final stretch of the domain, with a shear stress of 170 Pa. It is observed that the first Lagrangian method results in the highest values in both cases, while the other numerical methods present approximate values. In addition, it is notable that the PLI presents a behavior similar to the HI, with different values.

For the studied conditions, Eulerian analysis method did not present significant differences in relation to the experimental results, as well as the majority of studied Lagrangian methods. It is important to note that the Couette flow has a constant strain rate. Possibly the limitations of the Eulerian approach become accentuated for more complex flows, in which there are shear stress variations along the streamline.

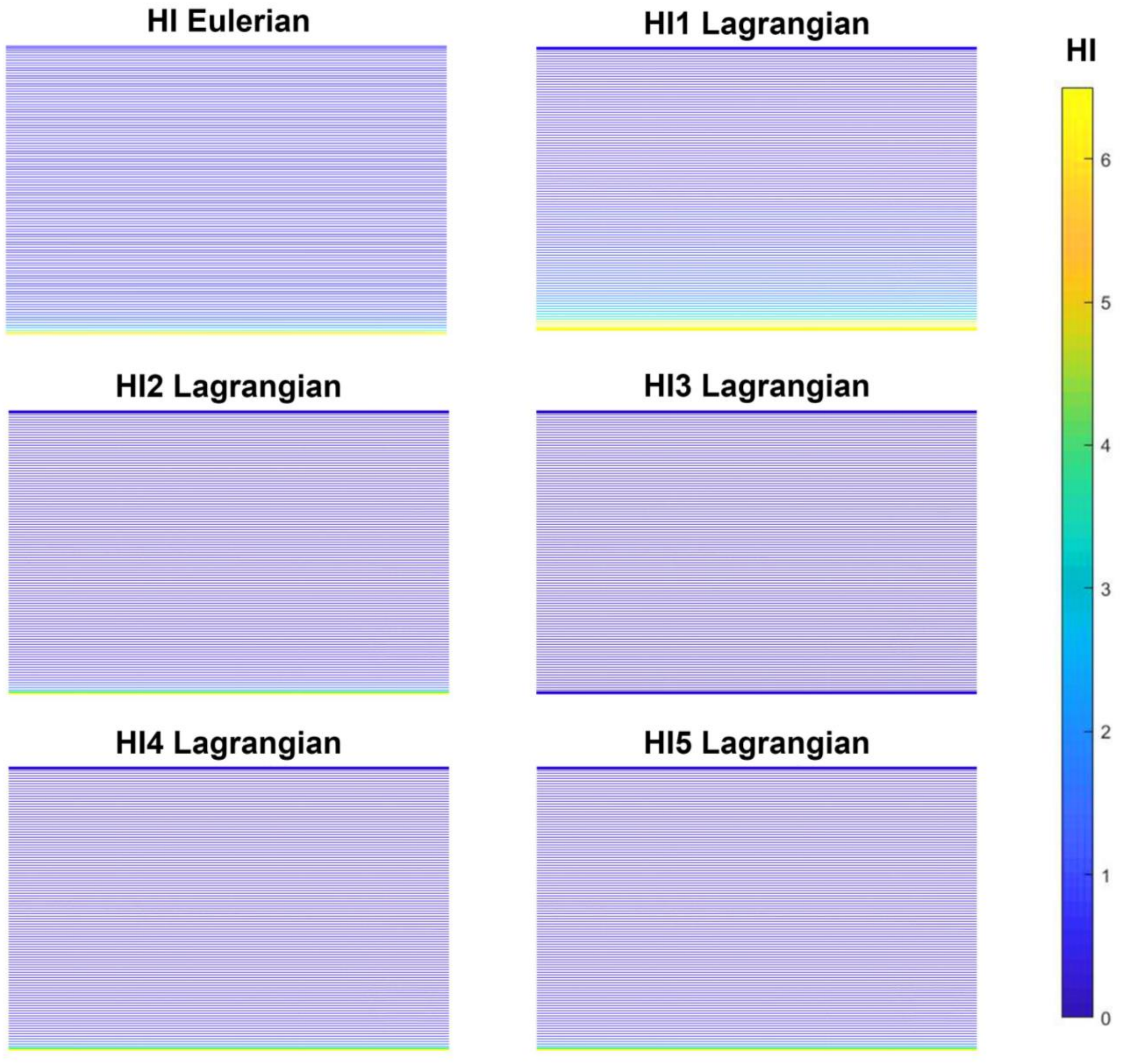

Figure 2. Streamlines of the numerical models of HI with a shear stress of 170 Pa in a Couette flow.

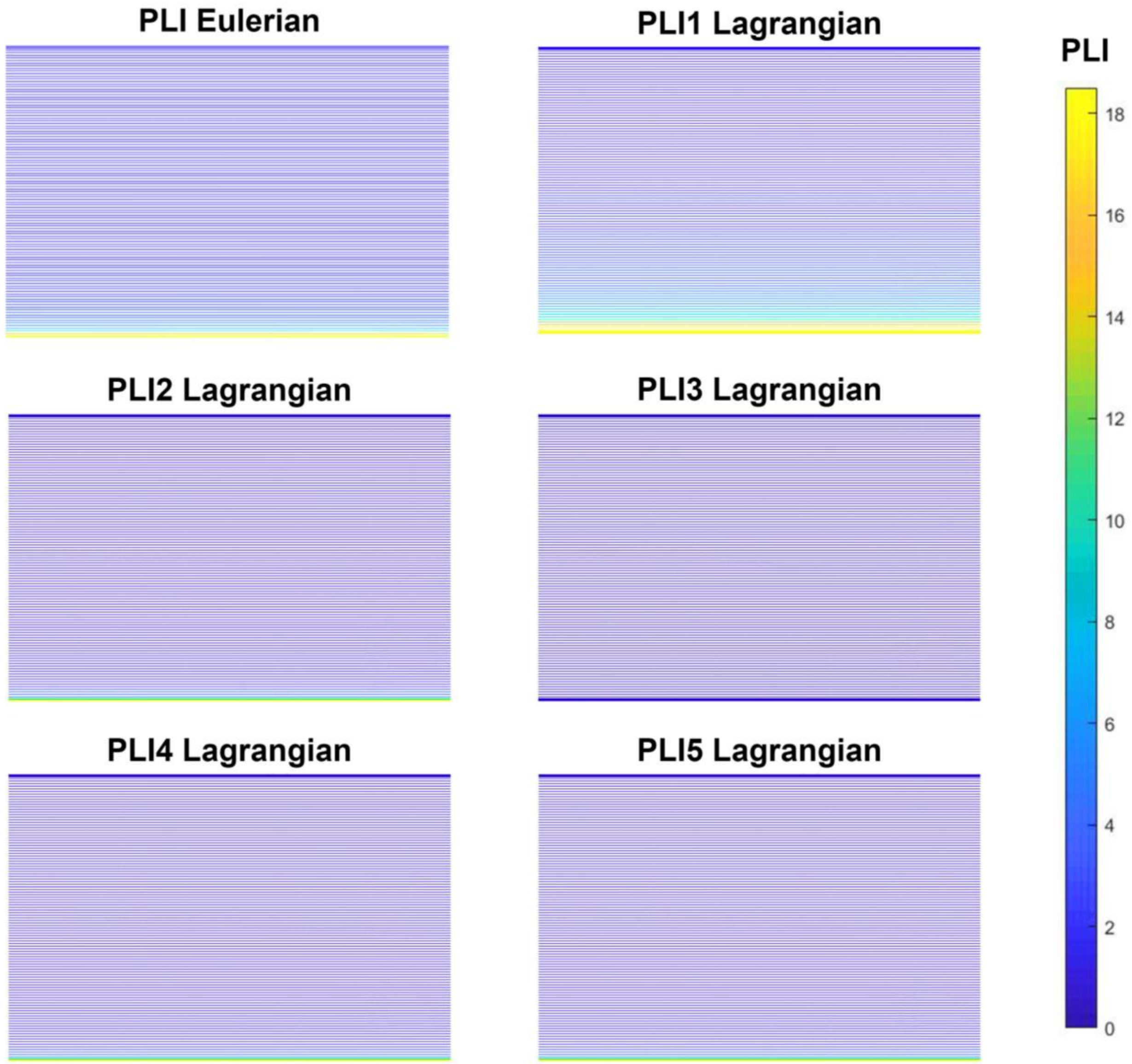

Figure 3. Streamlines of the numerical models of PLI with a shear stress of 170 Pa in a Couette flow.

4. CONCLUSION

Although contested by the limitations, the Eulerian approach in the Couette flow was able to represent the hemodynamic phenomena. In general, the errors between the mathematical models presented and experimental values were low. As the first Lagrangian method was the only one to present very high errors, this proved to be inadequate for the case studied.

The results of this study demonstrated possibility of using the Eulerian and the Lagrangian approaches in numerical simulations of blood flow by analyzing medical devices, considering simple flow. However, for the analysis of cardiac assistance systems with more complex flows, with great variation of speed in the streamline, a deeper analysis is necessary.

5. ACKNOWLEDGEMENTS

The authors would like to acknowledge Conselho Nacional de Desenvolvimento Científico e Tecnológico - CNPq (312982/2017-8) for its support in this research.

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