Grid convergence study for the prediction of hemolysis in blood circulatory devices: sensitivity to the form of equivalent stress and turbulence simulation methods

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Title page

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Abstract

Hemolysis and related complications induced by non-physiological stress are major concerns during the development and clinical applications of blood circulatory devices. Turbulence is one of the primary causes of hemolysis. To consider turbulence effects on hemolysis, various turbulence simulation methods and stress forms were employed or proposed. Nonetheless, the results showed significant divergence for different stress forms and turbulence simulation methods, discrediting hemolysis prediction as an important tool for the design, optimization and evaluation of blood circulatory devices. This study aims at quantitatively investigating the grid convergence for the prediction of hemolysis in blood circulatory devices, with a focus on its sensitivity to the stress forms and turbulence simulation methods. We revealed the integral of equivalent stress has very different characteristics of grid convergence. For Reynolds-averaged Navier-Stokes (RANS) method, grid convergence was less demanding on grid size and insensitive to stress forms. For large eddy simulation (LES), grid convergence was demanding and sensitive to stress forms, with highest uncertainty for the “total scalar stress”, followed by “viscous stress”. The “energy-dissipation stress” showed the best grid convergence for both RANS and LES. We also observed a significant divergence for metrics based on “total scalar stress” under different turbulence simulation methods, while the “energy-dissipation stress” showed a much higher consistency. We show the combination
of energy-dissipation stress and LES can better capture the trend of hemolysis and has the best grid convergence. This study provides insights for a better prediction of hemolysis in turbulent flows in blood circulatory devices.

**Keywords**  Hemolysis · Grid convergence · RANS · LES · Equivalent stress · Energy dissipation
1 Introduction

In mechanical-circulatory-support devices, such as prosthetic heart valves, ventricular assist devices (VADs) and hemodialysis machines, non-physiological stresses can be up to two orders of magnitude than normal physiological stresses (Fraser et al. 2010; Garon et al. 2004). Excessive stress can lead to hemolysis, thrombus, platelet and von Willebrand Factor (vWF) activation and other blood damage. Hemolysis is considered the most predominant form of blood damage in most VADs, which refers to the rupture of red blood cells and the release of hemoglobin into plasma. Typical power-law models consider hemolysis as a function of equivalent stress, or effective stress $\tau_{\text{eff}}$ and exposure time $t$ (Giersiepen et al. 1990; Heuser et al. 1980; Wu et al. 2018; Zhang et al. 2015):

$$HI(\%) = \frac{h_b}{H_b} \times 100 = C \tau_{\text{eff}}^{\alpha} t^{\beta},$$

where $HI(\%)$ is the hemolysis index in percentage; $h_b$ represents the increase in plasma-free hemoglobin and $H_b$ represents the total hemoglobin concentration. $C, \alpha$ and $\beta$ are empirical constants. $\tau_{\text{eff}}$ is scalar stress, which replaces all components of the real fluid stress tensor in complex flows (Bludszuweit 1995). A common practice is to use an equivalent scalar based on the second invariant of the strain-rate tensor (Hund et al. 2010). The equivalent stress is generally considered to be a function of the fluid viscosity and the second invariant of the strain-rate tensor (Pauli et al. 2013):
\[ \tau_{eff} = \mu \sqrt{2S_{ij}S_{ij}}, \]  

(2)

where \( \mu \) is the dynamic viscosity, \( S_{ij} \) is the strain rate tensor and given as:

\[ S_{ij} = \frac{1}{2} \left( \frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} \right). \]  

(3)

The power-law model was originally proposed to predict hemolysis in laminar flow. However, turbulence commonly exists in blood pumps and other blood circulatory devices (Wu et al. 2021). Reynolds number (Re) in blood pumps is in the range of \( 10^5 \sim 10^6 \), corresponding to transitional and low-Re flow regimes. For centrifugal blood pumps, as noted in Fraser et al. 2012; Taskin et al. 2010; Wu et al. 2021, due to the existence of the secondary flow path, turbulent intensity and recirculation is strong. When applied to turbulent flows, the complete prediction of the strain rate in Eq. 3 requires the Kolmogorov scales to be resolved, which can only be achieved by direct numerical simulations (DNS). Nonetheless, the computational cost of DNS is prohibitive. Thus, to reduce computational cost, turbulence models such as Reynolds-averaged Navier-Stokes (RANS) (Li et al. 2018; Wu et al. 2019; Wu et al. 2021) and recently, large eddy simulation (LES) (Huo et al. 2021; Wu et al.2011; Xiang et al. 2023), are commonly applied to blood pumps. Turbulence modeling techniques model small-scale motions while resolve large-scale motions. Unresolved turbulence motions are accounted for through Reynolds stress, which is related to strain rate according to the Boussinesq approximation (Kang 2008).
\[ \tau_t = 2\mu_t \bar{S}_{ij}, \quad (4) \]

where \( \bar{S}_{ij} \) represents resolved strain-rate tensor.

To consider turbulence effects and the unresolved turbulence motions, equivalent stress was often computed by adding up the viscous stress and Reynolds stress (total scalar stress):

\[ \tau_{eff} = (\mu + \mu_t) \sqrt{2 \bar{S}_{ij} \bar{S}_{ij}}. \quad (5) \]

Nonetheless, as previous studies showed (Hund et al. 2010; Wu et al. 2019; Wu et al. 2020), it is not a true representation of the original form of equivalent stress (Eq. 2), and tend to overpredict hemolysis in turbulent flows. Given the unsatisfactory performance of equivalent stress as defined in Eq. 5, another common practice is to leave out the term of Reynolds stress and just keep the viscous stress (Gross-Hardt et al. 2019a, b; Mantegazza et al. 2022). The overprediction of hemolysis was improved to some extent, but the correlation of predicted hemolysis and experimental results was even worse (Wu et al. 2020). Konnigk et al. (2021) confirmed that small-scale turbulent vortex not resolved by turbulence model should also be included in the range of equivalent stress. But they did not verify the accuracy of this form of stress for predicting hemolysis trends. Wu et al. (2020) confirmed that Reynolds stress was the main cause of excessive prediction of hemolysis. Wu et al. (2019) showed that the original form
of equivalent stress can be reformulated in terms of energy dissipation, which can be readily obtained from CFD simulations:

\[ \tau_{eff} = \sqrt{\rho \mu \varepsilon_{tot}}, \]  

(6)

where \( \rho \) is blood density, \( \varepsilon_{tot} \) is total energy dissipation. Their results showed that the representation of equivalent stress in terms of energy dissipation improved the over prediction of hemolysis remarkably, in terms of both absolute values and correlations with experimental results. Nonetheless the mechanism why the energy-dissipation stress improved hemolysis prediction over total scalar stress (cf. Eq. 5) was not elaborated in Wu et al. 2019 or Wu et al. 2020. Moreover, RANS methods were employed to model turbulence in their studies. Turbulence modeling technique is one of the crucial factors which affects the prediction of stress and hemolysis (Blocken 2018; Heinz 2020). RANS is known for its deficiency for capturing circulation and separation flows which are commonly exist in blood pumps, leading to an inaccurate prediction of pump performance such as pressure head (Huo et al. 2021). LES is superior in capturing these flows, performing well for both design and off-design conditions. Bozzi et al. (2021) compared the results of platelet activation between different turbulence models including laminar, RANS, LES and DNS. Their results showed that the small and fast flow structure in the separation zone could only be captured by LES and DNS. The sensitivity of pressure head and viscous stress to the grid under different turbulence models could be found in the study by Gross-Hardt et al. 2019b. The
result of SST k-ω was least sensitive to the grid. Nevertheless, it was unreasonable to compare only the viscous stress when mean y+ is larger than 4. The Reynolds stress was no longer negligible outside the viscous bottom layer. Torner et al. (2018) studied the difference in the prediction of viscous shear between RANS and LES methods. They pointed out that LES was much superior to RANS in terms of the resolution of the instantaneous stresses, which could be a key element to numerically predict blood damage. Nevertheless, only viscous stress was compared and why the predicted hemolysis under LES method was higher than RANS method lacked effective validation. Thus, LES method should be employed to provide more accurate input for hemolysis prediction, and the effect of turbulence modeling technique on hemolysis prediction should be further investigated.

As one of the uncertain factors of computational fluid dynamics (CFD), grid has a very important influence on the prediction of equivalent stress and hemolysis (Wu et al. 2022). Lopes et al. (2016) investigated the relationship between pressure head and the grid size for a ventricular assist device. They found that the change of pressure head was not obvious only when grid size increased beyond a certain threshold. However, grid convergence of hemolysis was not demonstrated. Gross-Hardt et al. (2019a) studied the variation of wall shear stress with $y^+$ for RANS simulations. Their results showed that grid convergence solutions required $y^+$ less than 0.1 for wall shear stress and for $y^+$
less than 0.2 for hemolysis. However, turbulence effect was neglected when calculating the equivalent stress. Konnigk et al. (2018) investigated the relationship between the integral of equivalent stress (considering only the viscous stress) and grid size. They found grid size had a significant effect on the integral of equivalent stress. The numerical uncertainty of the stress on the grid was high up to 20%, which was much larger than the 4.8% of the pressure head. Nevertheless, the grid size for a converged integral of equivalent stress was not determined in their study. The integration of stress had no physical meaning; the convergence of hemolysis source terms under different stress forms and different turbulence simulation methods seemed to be worthier to study.

This study aims to quantitatively investigate the grid convergence for the prediction of hemolysis in blood-contacting devices, with a focus on its sensitivity to the form of equivalent stress and turbulence modeling technique. In this study, different stress forms and turbulence simulation methods showed different grid convergence characteristics. The combination of energy-dissipation stress and LES can better capture the trend of hemolysis and had the best grid convergence. This study provides insights for a better prediction of hemolysis in turbulent flows in blood pumps.

2 Methods

2.1 Forms of equivalent stress
The aforementioned three forms of equivalent stress, i.e. viscous stress, total scalar stress (cf. Eq. (5)) and energy-dissipation stress (cf. Eq. (6)) are referred to as \( \tau_{\text{eff}1} \), \( \tau_{\text{eff}2} \) and \( \tau_{\text{eff}3} \) respectively:

\[
\tau_{\text{eff}1} = \mu \sqrt{2\bar{S}_{ij}\bar{S}_{ij}}, \tau_{\text{eff}2} = (\mu + \mu_t) \sqrt{2\bar{S}_{ij}\bar{S}_{ij}}, \tau_{\text{eff}3} = \sqrt{\rho \mu \varepsilon_{\text{tot}}},
\]

where \( \varepsilon_{\text{tot}} \) is the sum of resolved part of energy dissipation \( \varepsilon_{\text{res}} \) and modeled part of energy dissipation \( \varepsilon_{\text{mod}} \):

\[
\varepsilon_{\text{tot}} = \varepsilon_{\text{res}} + \varepsilon_{\text{mod}}.
\]

\( \varepsilon_{\text{res}} \) and \( \varepsilon_{\text{mod}} \) are given as Wu et al. 2019:

\[
\varepsilon_{\text{res}} = 2\nu \bar{S}_{ij}\bar{S}_{ij},
\]

and

\[
\varepsilon_{\text{mod}} = 2\nu_t \bar{S}_{ij}\bar{S}_{ij},
\]

respectively, where \( \nu = \mu / \rho \) and \( \nu_t = \mu_t / \rho \) are the kinematic viscosity and eddy kinematic viscosity. The energy-dissipation stress can be further rewritten as

\[
\tau_{\text{eff}3} = \sqrt{\rho \mu \varepsilon_{\text{tot}}} = \sqrt{\rho \mu (\varepsilon_{\text{res}} + \varepsilon_{\text{mod}})} = \sqrt{\rho \mu (\nu + \nu_t) \bar{S}_{ij}\bar{S}_{ij}} = \sqrt{\mu^2 + \mu\mu_t} \cdot 2\bar{S}_{ij}\bar{S}_{ij}.
\]
Introducing a non-dimensional number eddy viscosity ratio (EVR), defined as the ratio of \( \mu_t \) and \( \mu \), then we obtain:

\[
\begin{align*}
\tau_{eff2} &= (\mu + \mu_t) \sqrt{2\bar{S}_{ij} \bar{S}_{ij}} = \mu (1 + EVR) \sqrt{2\bar{S}_{ij} \bar{S}_{ij}}. \\
\tau_{eff3} &= \sqrt{\mu^2 + \mu \mu_t} \cdot \sqrt{2\bar{S}_{ij} \bar{S}_{ij}} = \mu \sqrt{1 + EVR} \sqrt{2\bar{S}_{ij} \bar{S}_{ij}}. \\
\tau_{eff2}/\tau_{eff3} &= \sqrt{1 + EVR}.
\end{align*}
\]

(12) (13) (14)

2.2 Test cases and grid setup

Two models, i.e. a capillary tube and the FDA nozzle model, were investigated for the prediction of flow quantities and hemolysis in transitional and Low-Re turbulent flows. Detailed descriptions of these two cases were given in Kameneva et al. (2004) and Giarra et al. (2011), as well as Wu et al. 2019 and Wu et al. 2020.

A set of grids were generated for each model. All grids were structured and were generated using Ansys ICEM CFD 2019R1 (Ansys, Inc., Canonsburg, PA, USA). The fine grids were created by proportionally refining coarse grids successively, starting from the coarsest grid. The grids were refined in each direction by the same ratio. The wall distance of the first grid was decreased with the same ratio. Thus, the \( \gamma^+ \) decreased accordingly. The metrics of grid quality were kept within the recommended range of the ICEM CFD guidelines, with the
minimal grid angle of 36° and more than 99% of the grid angles larger than 36°. Each model was simulated under several different conditions and with a different number of grids.

### 2.2.1 Capillary tube

The structure of capillary tube is shown in Fig.1, which was firstly used by Kameneva et al. (2004), with hemolysis experimental results available. The diameter of the tube was 1 mm with a length of 70 mm. Conical connectors with a length of 8 mm were fitted on both sides to reduce the entrance and exit effects. Three conditions were considered in this study, with Reynolds numbers ranging from 3500 to 5100, as shown in Table 1.

![Fig.1 Schematic of capillary tube](image)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Flow rate (L/min)</th>
<th>$Re_d$</th>
<th>Measured HI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.33</td>
<td>3500</td>
<td>$9.39 \times 10^{-4}$</td>
</tr>
<tr>
<td>2</td>
<td>0.42</td>
<td>4500</td>
<td>$3.79 \times 10^{-3}$</td>
</tr>
<tr>
<td>3</td>
<td>0.48</td>
<td>5100</td>
<td>$8.50 \times 10^{-3}$</td>
</tr>
</tbody>
</table>

Reynolds number $Re_d$ was calculated based on average velocity and tube diameter.
Eight grids were generated and listed in Table 2. Among them, “R-1” to “R-5” were for RANS studies, while “L-1” to “L-5” were for LES studies. The “R-4” and “R-5” were the same grids as the “L-1” and “L-2”, and used for both RANS and LES studies. $y^+$ were kept within 2 for all the RANS grids and within 1.5 for the LES grids. The “R-4” or “L-1” grid is shown in Fig 2.

<table>
<thead>
<tr>
<th>Grid label</th>
<th>Grid size (million)</th>
<th>Average grid spacing(m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tubu_R-1</td>
<td>0.22</td>
<td>$1.29 \times 10^{-4}$</td>
</tr>
<tr>
<td>Tubu_R-2</td>
<td>0.45</td>
<td>$1.01 \times 10^{-4}$</td>
</tr>
<tr>
<td>Tubu_R-3</td>
<td>1.01</td>
<td>$7.75 \times 10^{-5}$</td>
</tr>
<tr>
<td>Tubu_R-4/L-1</td>
<td>2.39</td>
<td>$5.82 \times 10^{-5}$</td>
</tr>
<tr>
<td>Tubu_R-5/ L-2</td>
<td>4.14</td>
<td>$4.84 \times 10^{-5}$</td>
</tr>
<tr>
<td>Tubu_L-3</td>
<td>8.25</td>
<td>$3.85 \times 10^{-5}$</td>
</tr>
<tr>
<td>Tubu_L-4</td>
<td>12.30</td>
<td>$3.37 \times 10^{-5}$</td>
</tr>
<tr>
<td>Tubu_L-5</td>
<td>16.60</td>
<td>$3.05 \times 10^{-5}$</td>
</tr>
</tbody>
</table>

![Fig.2](image) The “Tube_R-4/L-1" grid (2.39 million) at the inlet section

### 2.2.2 The FDA nozzle model

The FDA nozzle model has been widely employed to assess the quality of CFD and hemolysis predictions (see Fig.3), with both PIV (Hariharan et al. 2011)
and hemolysis (Herbertson et al. 2015) experimental results available. The nozzle model can be alternated to change flow directions, referred to as “sudden expansion model” and “conical diffuser model” respectively. The “conical diffuser model” generates significantly more hemolysis and was investigated in this study. Three conditions were studied, as listed in Table 3. PIV results were available for condition 1 only, which was investigated mainly for the purpose of validating the CFD prediction of the flow field; while hemolysis results were available for conditions 2 and 3.

![Fig.3 Schematic of the FDA nozzle model](image)

**Table 3** Overview of conditions studied for the FDA benchmark nozzle model

<table>
<thead>
<tr>
<th>Condition</th>
<th>Flow rate(L/min)</th>
<th>Re$_d$</th>
<th>Measured HI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.1</td>
<td>6500</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>6650</td>
<td>2.92 x 10$^{-5}$</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>8020</td>
<td>1.239 x 10$^{-4}$</td>
</tr>
</tbody>
</table>

Reynolds number Re$_d$ was calculated based on average velocity and throat diameter.

Eight sets of grids were listed as Table 4. Among them, “R-1” to “R-5” were for RANS studies, while “L-1” to “L-5” were for LES studies. The “R-4” and “R-5” were the same grids as the “L-1” and “L-2”, and used for both RANS and LES.
studies. $y^+$ were kept within 2 for all the RANS cases and LES cases. The R-L-4/L-1 grid is shown in Fig. 4.

<table>
<thead>
<tr>
<th>Grid label</th>
<th>Grid size (million)</th>
<th>Average grid spacing (m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nozzle_R-1</td>
<td>0.24</td>
<td>$4.80 \times 10^{-4}$</td>
</tr>
<tr>
<td>Nozzle_R-2</td>
<td>0.51</td>
<td>$3.73 \times 10^{-4}$</td>
</tr>
<tr>
<td>Nozzle_R-3</td>
<td>1.06</td>
<td>$2.93 \times 10^{-4}$</td>
</tr>
<tr>
<td>Nozzle_R-4/L-1</td>
<td>2.44</td>
<td>$2.22 \times 10^{-4}$</td>
</tr>
<tr>
<td>Nozzle_R-5/L-2</td>
<td>4.97</td>
<td>$1.75 \times 10^{-5}$</td>
</tr>
<tr>
<td>Nozzle_L-3</td>
<td>8.80</td>
<td>$1.44 \times 10^{-5}$</td>
</tr>
<tr>
<td>Nozzle_L-4</td>
<td>13.16</td>
<td>$1.26 \times 10^{-5}$</td>
</tr>
<tr>
<td>Nozzle_L-5</td>
<td>19.02</td>
<td>$1.12 \times 10^{-5}$</td>
</tr>
</tbody>
</table>

**Fig. 4** The “Nozzle_R-4/L-1” grid (2.44 million) near the throat

### 2.3 CFD analysis

All simulations were conducted using the commercial software Ansys Fluent 2019R1. Blood was simulated as incompressible Newtonian fluid with a density of $1050 \text{kg/m}^3$ and dynamic viscosity $3.5 \text{mPa}\cdot\text{s}$. Two turbulence models were employed: the SST $k$-$\omega$ and Wall-modeled LES (WMLES). Although the WMLES
still requires the value $y^+$ within 1, it relaxes the stringent requirements for grid resolution in wall-parallel directions and operates in a RANS-alike mode near wall. Thus, it can reduce computational cost for medium to high Reynolds number wall bounded flows. Velocity inlet and pressure outlet boundary conditions were adopted in all the cases. In each case the time step was adjusted accordingly to the grid size to meet the requirement that the cell Courant number is less than 1 in the full fluid domain. SIMPLE algorithm and pressure-based method were used for calculation. Both spatial and time accuracy were second-order. All the simulations were transient, with a maximum of 25 sub-iterations for each physical time step. Convergence criteria were set that the residuals of the all equations drop by 3 magnitudes, and monitored values such as pressure difference, axial velocity etc. were in a statistically steady state for a period of time.

2.4 Hemolysis calculation

The power-law hemolysis model (cf. Eq. 1) was used to predicted hemolysis and applied through a Eulerian scalar transport approach (Garon et al. 2004). Let

$$D_t = D^\frac{1}{\beta} = C^\frac{1}{\beta} \tau^\alpha t .$$  \hspace{1cm} (15)

Then

$$\frac{dD_t}{dt} = \left( \frac{\partial}{\partial t} + \bar{u} \cdot \nabla \right) D_t = C^\frac{1}{\beta} \tau^\alpha t^\frac{\alpha}{\beta} = \sigma ,$$  \hspace{1cm} (16)
where $\sigma$ represents source term for hemolysis prediction. Ignore the unsteady effects and take the volume integration on both sides of Eq. (16), then

$$\int_Y (\bar{u} \cdot \nabla) D_I dV = \int_Y (\bar{u} \cdot \bar{n}) D_I dS = Q D_I = \int_Y \sigma dV = S. \quad (17)$$

We defined $S_1$, $S_2$ and $S_3$ as the volume integrals corresponding to the stress forms of $\tau_{eff1}$, $\tau_{eff2}$ and $\tau_{eff3}$, respectively. Hemolysis at the outlet of the computational domain could be obtained as

$$HI(\%) = D = (D_I)^\beta = \left(\frac{1}{Q} \int_Y \sigma dV\right)^\beta. \quad (18)$$

Hemolysis computed according to Eq. 18 was a rough estimate of hemolysis since unsteady term was neglected. Nonetheless, the error was acceptable since the unsteadiness of the investigated flows in this study was not pronounced.

### 3 Results

#### 3.1 Capillary tube

Fig. 5 shows variation of $S$ (volume integral of the source term $\sigma$, cf. Eq. 16) with grid size using RANS method. It was considered that the convergence had been achieved if the difference between the solutions of two adjacent grids was less than 3%. With the refinement of the grid, the values changed, and grid convergence was reached when the average grid size decreased to 7.75E-5m (corresponding to “R-3”) for all forms of equivalent stress and Reynolds numbers.
Fig. 5 Variation of the $S = \int \sigma dV$ in the capillary tube using RANS method for different Re and stress forms: (a) $\tau_{eff1}$, (b) $\tau_{eff2}$ and (c) $\tau_{eff3}$

The variation of $S$ with grid size using LES method is shown in Fig. 6. Unlike RANS, the three stress forms showed different grid convergence characteristics. For $\tau_{eff2}$, grid convergence was not reached. The variation of $S$ with grid size was more pronounced compared with RANS. Reynolds number also had greater influence on the convergence compared to RANS method. With the increase of Reynolds number, the grid size required to reach grid convergence increased (see Fig 7(a)&(c)). A noteworthy phenomenon was that $S$ showed a different convergence trend than that under RANS method at the coarsest grid “L-1” for
τ_{eff2} and τ_{eff3}. In other words, the curves were monotonic only from grid “L-2” to “L-5”. The reason will be discussed in detail in the next section.

Fig.6 Variation of the $S$ in the capillary tube using the LES method for different Re and stress forms: (a) $\tau_{eff1}$, (b) $\tau_{eff2}$ and (c) $\tau_{eff3}$

Fig.7 shows the eddy viscosity ratio (EVR) for three conditions (Re) on the finest grids for RANS (“R-5” grid) and LES respectively (“L-5” grid). For RANS, except for the gradual contraction and front part of the throat, the EVR was larger than 1 in most regions, while for LES, The EVR was less than 0.1 at most regions of the flow field, including the entire throat section. The region where the EVR exceeded 1 mainly located downstream of the expansion, where jet broke. The
position of jet broke moved upstream as Re increased. This indicates that for RANS, a great part of the turbulent field was modeled, while for LES, most of the turbulent field was resolved.

![Eddy viscosity ratio contours at different Reynolds numbers obtained using RANS (above) and LES (below) on respective finest grid ("R-5" grid for RANS, "L-5" grid for LES), for the capillary tube.](image)

Table 5 shows volume-averaged EVR for the capillary tube. Both the EVR increased with the Reynolds number. As Re increased, modeled part of turbulent flow field would increase, leading to a higher $\mu_t$ and EVR. The EVR of RANS
method were more than one order higher than LES, leading to an apparent disparity of the $S_2/S_3$ between RANS and LES methods (cf. Fig.5 and Fig.6).

**Table 5** Volume-averaged EVR obtained using RANS and LES on respective finest grid ("R-5" and "L-5" grids) for the capillary tube

<table>
<thead>
<tr>
<th>Condition</th>
<th>RANS</th>
<th>LES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5.200</td>
<td>0.086</td>
</tr>
<tr>
<td>2</td>
<td>6.886</td>
<td>0.126</td>
</tr>
<tr>
<td>3</td>
<td>7.886</td>
<td>0.155</td>
</tr>
</tbody>
</table>

for the total scalar stress $\tau_{eff2}$, the $S_2$ and corresponding hemolysis using the LES method has not reach grid convergence on “L-5” grid

The predicted hemolysis on grid “R-5” and “L-5” (the finest grid for RANS and LES respectively) is shown in Fig. 8, in comparison with experimental results. Only the predicted hemolysis using Heuser constants (Heuser et al. 1980) is shown here, since we found that adopting different sets of power-law constants did not lead to different conclusions. The overall level of predicted hemolysis using LES were lower than that using RANS, despite that the results were closer on the $\tau_{eff1}$. For both RANS and LES, the hemolysis based on $\tau_{eff2}$ was the highest, followed by $\tau_{eff3}$. The hemolysis values based on $\tau_{eff1}$ were the lowest. All the predicted hemolysis over-predicted hemolysis, the hemolysis
based on $\tau_{eff3}$ & $\tau_{eff1}$ and predicted using LES were the closest to experimental results.

Table 6 lists the correlation coefficients of predicted hemolysis and experimental results for the capillary tube. The hemolysis based on $\tau_{eff3}$ using LES had the highest correlation with the experimental value. Using viscous stress $\tau_{eff1}$ to account for hemolysis seemed to reluctantly feasible to some extent.

![Fig.8 Predicted HI(%) for capillary tube using various equivalent stress forms under different turbulence method, in comparison with experimental results](image)

<table>
<thead>
<tr>
<th>Methods</th>
<th>$\tau_{eff1}$</th>
<th>$\tau_{eff2}$</th>
<th>$\tau_{eff3}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>RANS</td>
<td>0.9671</td>
<td>0.9698</td>
<td>0.9278</td>
</tr>
<tr>
<td>LES</td>
<td>0.9672</td>
<td>/</td>
<td>0.9769</td>
</tr>
</tbody>
</table>
3.2 FDA nozzle model

Fig. 9 shows the velocity and pressure along centerline on different grids in comparison with experimental results. The results were relatively insensitive to grid resolution, except for the pressure of LES in the throat, which were closer to experimental results with grid refinements. The RANS failed to capture the location of jet breakup, while the LES captured it well on all its grids (cf. Fig. 9(b)&(d)). This is probably due to the inherent incapability of RANS to capture the detachment of boundary layer and decelerating flows in the diffuser.

![Fig.9 Predicted velocity and pressure distributions along the centerline for condition1 (Re=6500): (a)&(b) RANS results, (c)&(d) LES results](image-url)
Fig. 10 shows the variation of $S$ with grid size for the FDA nozzle at condition 1 (cf. Table 3). For RANS method, the curves were quite flat, while for LES method, different grid convergence characteristics could be observed for different forms of equivalent stress. The $\tau_{eff3}$ curve was the flattest, with grid convergence occurring at grid “Nozzle_ L-2”, and the $\tau_{eff1}$ curve converged at “Nozzle_ L-4”, while $\tau_{eff2}$ did not converge.

Fig. 10 Variation of the $S$ in FDA nozzle model for stress forms using (a) RANS, and (b) LES

Fig. 11 shows the predicted hemolysis in the FDA nozzle model, in comparison with experimental results. The ratio of experimental hemolysis between the two conditions was 4.24. For both RANS and LES, the hemolysis based on $\tau_{eff2}$ were the highest and the values based on $\tau_{eff1}$ were the lowest. All the predicted hemolysis over-predicted hemolysis, too.

Comparison in terms of the absolute hemolysis values with experiment is of little significance, according to previous studies (Craven et al. 2019; Mantegazza
et al. 2022; Wu et al. 2019). The trend of hemolysis and its correlation with experimental results are more important (Mantegazza et al. 2022; Wu et al. 2019). Table 7 lists the ratio of hemolysis at condition 2 and 3 of the FDA nozzle model (cf. Table 3) using different turbulent modeling methods. All the predicted ratios were lower than the experiment results, while the ratio based on $\tau_{eff3}$ and LES (3.11) was the closest to experimental results. This was consistent with the case of capillary tube (cf. Table 6).

![Fig.11](image_url) Predicted $HI(\%)$ for the FDA nozzle model using various equivalent stress forms under different turbulence method, in comparison with experimental results

**Table 7** $HI_{6L}/HI_{5L}$ for the FDA nozzle using different turbulence modeling methods

<table>
<thead>
<tr>
<th>Methods</th>
<th>$\tau_{eff1}$</th>
<th>$\tau_{eff2}$</th>
<th>$\tau_{eff3}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>RANS</td>
<td>1.01</td>
<td>1.75</td>
<td>1.21</td>
</tr>
<tr>
<td>LES</td>
<td>1.33</td>
<td>1.89</td>
<td>3.11</td>
</tr>
</tbody>
</table>

**4 Discussion**
In this research, the grid convergence of hemolysis prediction was investigated, with a focus on its sensitivity to forms of equivalent stress and turbulence modeling methods. This study reveals that the integral of equivalent stress has very different characteristics of grid convergence, depending on turbulence modeling technique, form of equivalent stress and Reynolds number. Table 8 lists the uncertainty of $S$ for different turbulence methods and stress forms. For RANS method, grid convergence was less demanding on grid size and insensitive to stress forms. While for LES method, grid convergence was much more demanding compared with RANS and sensitive to stress forms. For RANS method, the highest uncertainty occurred at condition 3 when using $\tau_{eff2}$ for the capillary tube, but was only of 15.6%. For LES method, this uncertainty was much higher and up to 166.9% for $\tau_{eff2}$ at the same condition. This indicates that $\tau_{eff2}$, the total scalar stress, was most sensitive to grid resolution using LES method. The energy-dissipation equivalent stress $\tau_{eff3}$ showed the best grid convergence for both RANS and LES, with uncertainties below 20%.

**Table 8** Uncertainty of $S$ for capillary tube and FDA nozzle model under different turbulence methods and stress forms

<table>
<thead>
<tr>
<th>Condition</th>
<th>RANS</th>
<th></th>
<th></th>
<th>LES</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$U_{1,R}$</td>
<td>$U_{2,R}$</td>
<td>$U_{3,R}$</td>
<td>$U_{1,L}$</td>
<td>$U_{2,L}$</td>
<td>$U_{3,L}$</td>
</tr>
<tr>
<td>Tube_1</td>
<td>8.3</td>
<td>11.8</td>
<td>10.8</td>
<td>13.6</td>
<td>121.2</td>
<td>15.6</td>
</tr>
<tr>
<td>Tube_2</td>
<td>8.6</td>
<td>12.0</td>
<td>12.3</td>
<td>29.9</td>
<td>125.6</td>
<td>16.4</td>
</tr>
</tbody>
</table>
The uncertainty $U$ is calculated according to $\left| \frac{S_{\text{max}} - S_{\text{min}}}{S_{\text{min}}} \right| \times 100\%$, where $S_{\text{max}}$ and $S_{\text{min}}$ represent the maximum and minimal value of $\int_{V} \sigma dV$ from grid 1 to 5.

For RANS method, more turbulence motions were modeled compared with LES, resulting in a much higher $\mu_t$ and EVR (approximately 50 to 60 times that of LES, cf. Fig. 5&Table 5). Recall that $\tau_{eff2}/\tau_{eff3} = \sqrt{1 + EVR}$ (cf. Eq. 14). This explains that a much higher $S_2/S_3$ (see Table 8) and over-prediction of hemolysis when using $\tau_{eff2}$ (cf. Wu et al. 2019, Fig. 8&11) for RANS than LES. As Re increased (from condition “Tube_1” to “Tube_3”, cf. Table 5), the $S_2/S_3$ increased as well for both RANS and LES (see “$S_{2,R}/S_{3,R}$” and “$S_{2,L}/S_{3,L}$” in Table 8), due to increasing $\mu_t$ at higher Re. It can also be observed that $S_3$ was much closer between RANS and LES compared with $S_2$. This was in line with Fig. 8&11, which showed that the predicted $HI(\%)$ based on $\tau_{eff3}$ were much closer for RANS and LES, while the predicted $HI(\%)$ based on $\tau_{eff2}$ using RANS were several times higher than that by LES. Similar observations were also reported by Konnigk et al. 2021. For RANS, although a large portion of turbulence dissipation was modeled, the total dissipation or flow loss was not very different from the LES, or even DNS (Konnigk et al. 2021). Thus, the predicted $S$ or $HI(\%)$ (based on $\tau_{eff3}$) as a function of volume integral of total energy dissipation were also close to each other for different turbulence modeling methods. In contrast,
volume integral of $S_2$ does not correspond to any physical quantities of practical meaning. Thus, $S_2$ and the corresponding $HI(\%)$ showed significant divergence for different turbulence modeling methods. This indicates that $\tau_{eff2}$, the total scalar stress, could be a wrong indicator to predict the hemolysis, especially when used in combination with RANS.

**Table 9** Comparison of $S$ considering forms of equivalent stress ($S_{2,R}/S_{3,R}$, $S_{2,L}/S_{3,L}$) and turbulence modeling methods ($S_{2,R}/S_{2,L}$, $S_{3,R}/S_{3,L}$), on respective finest grids ("R-5" for RANS and "L-5" for LES)

<table>
<thead>
<tr>
<th>Condition</th>
<th>$S_{2,R}/S_{3,R}$</th>
<th>$S_{2,L}/S_{3,L}$</th>
<th>$S_{2,R}/S_{2,L}$</th>
<th>$S_{3,R}/S_{3,L}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tube_1</td>
<td>10.61</td>
<td>2.46</td>
<td>7.33</td>
<td>1.70</td>
</tr>
<tr>
<td>Tube_2</td>
<td>13.97</td>
<td>3.66</td>
<td>6.57</td>
<td>1.72</td>
</tr>
<tr>
<td>Tube_3</td>
<td>15.99</td>
<td>4.50</td>
<td>6.04</td>
<td>1.70</td>
</tr>
<tr>
<td>Nozzle_1</td>
<td>83.03</td>
<td>2.69</td>
<td>33.83</td>
<td>1.09</td>
</tr>
</tbody>
</table>

The subscript “$R$” stands for the RANS method, while “$L$” stands for the LES method.

One should note that grid convergence had not been fully reached for $\tau_{eff2}$ under LES method. The high uncertainty of $\tau_{eff2}$ using LES method was partially due to the fact that the result of “L-1” was not within the convergence range. For tube condition 3 with a Re of 5100, the volume average of eddy viscosity was 0.000426 Pa·s on the “L-1” grid, while from “L-2” to “L-5” this value monotonically decreased from 0.000753 to 0.000542 Pa·s. The reason might be
that the “L-1” grid was too coarse to satisfy the basic requirement for spatial resolution. Some studies have pointed out that the results predicted by LES are better than RANS, even with the same spatial and temporal resolution (Huo et al. 2021; Konnigk et al. 2018). However, as this study shows, adequate grid resolution should be achieved to ensure that the results of LES are within the convergence range.

As the grids continue to be refined until grid resolution approaches the requirement of DNS, most of turbulent scales will be resolved and the impact of $\mu_t$ will be minimal and negligible for the LES. $S_1$, $S_2$ and $S_3$ will be very close overall by then. However, for RANS method, $\mu_t$ is almost independent of grid spacing, further grid refinement will not bring $S_2$ and $S_3$ closer. One should also note the WMLES was employed in this study, which is technically a hybrid LES/RANS method, with RANS mode and grid resolution applied at the inner layers. The rate of grid convergence for wall-resolved LES (WRLES) might be faster than the WMLES. The difference between $S_1$ and $S_2$ might also be larger than the WMLES. However, the size of the finest grids used to calculate $S_2$ in our study (“L-5” grids) was decent (15~20 million), and had reached or even exceeded the grid size of many studies involving blood pumps, for which the Re is much higher than the Re investigated in this study (Manchester et al. 2020; Mantegazza et al. 2022). Thus, it will be difficult to obtain a grid convergent solution for the stress form of $\tau_{eff2}$ using LES method, especially for high-Re
blood circulatory devices such as blood pumps. When predicting hemolysis using LES methods, the grid sensitivity analysis should be approached with caution and always include hemolysis as one the critical metrics.

In this research, the energy-dissipation stress showed the best grid convergence for both RANS and LES. We also observed a significant divergence for metrics based on “total scalar stress” under different turbulence simulation methods, while the “energy-dissipation stress” showed a much higher consistency. To sum up, LES method combined with the energy-dissipation equivalent stress can better capture the trend of hemolysis and has the best grid convergence. It is a viable and relatively accurate method for the prediction of hemolysis using the stress-based hemolysis models. This study provides useful insights for a better prediction of hemolysis in turbulent flows in blood circulatory devices.

5 Limitation

The conditions of the two cases investigated in this study covered only the lower Reynolds number range. Reynolds number can be up to the order of $10^5$ for blood pumps. In these cases, the flow will be much more turbulent. The aforementioned disparity between metrics associated with different forms of effective stress and turbulence modeling method will be presumably more pronounced. Nonetheless, this will not change the conclusions of this study. In
future study, it is worthy to investigate the degree of grid refinement when the
difference between different stress forms under LES method are no longer
significant.

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Declarations

Conflicts of interest The authors declare that they have no conflict interest.

Data availability statement

Research data are not shared.
References


