Chapter 7

The Influence of Flow, Vessel Diameter and Non-Newtonian Blood Viscosity on the Wall Shear Stress in a Carotid Bifurcation Model for Unsteady Flow

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Abstract

Objectives The atherosclerotic process in arteries is correlated with the local wall shear stress (WSS). Plaque development particularly occurs in regions with recirculation, i.e. where the WSS oscillates. We investigated the effects of non-Newtonian blood viscosity, the variations in flow rate and vessel diameter on wall phenomena in a carotid bifurcation model.

Materials and Methods The flow through a model of a carotid artery bifurcation was simulated by means of the Finite Element Method. The whole blood viscosity is a function of shear rate, and was modeled by the Carreau –Yasuda (CY) model. Flow rate and vessel morphology were assessed with magnetic resonance imaging (MRI). Flow rate, blood viscosity and haematocrit levels (Hct) were measured in 49 healthy volunteers. We propose an adaptation of the CY model so that differences in haematocrit can be incorporated; furthermore, plasma viscosity was varied in the CY-model.

Results The data from our model indicate that flow increases have a larger effect on the WSS than predicted with a simple paraboloid model. Hct had more influence on the WSS when the plasma viscosity was low. Low plasma viscosity was associated with a low WSS, which implies a contradiction, because both high WSS and low plasma viscosity are thought to be indicators for a healthy system. Maximum WSS oscillations were found at the edges of the recirculation region.

Conclusions Flow and diameter changes have significant influence on wall shear stress values; the same is true for the viscosity, but to a lesser extent.
7.1 Introduction

It is well known that a correlation exists between the presence of atherosclerosis and the local wall shear stress (WSS) in arteries\(^1\). The WSS is defined as the mechanical frictional force exerted on the vessel wall by the flowing blood. The WSS \(\tau_w\) (Pa) is defined by the wall shear rate WSR \(\dot{\gamma}\) (s\(^{-1}\)) multiplied by the dynamic viscosity \(\eta\) (Pas). Near the vessel wall, \(\dot{\gamma}\) can be expressed as the fluid velocity gradient with respect to the outward normal \(n\) of the wall, or in other words

\[
\tau_w = \eta \dot{\gamma} = \eta \frac{\partial v}{\partial n},
\]

with \(v\) being the fluid velocity [m/s]. Several studies have been carried out to investigate the fluid dynamic differences in blood vessels between non-Newtonian and Newtonian viscosities\(^2-4\). Furthermore, the relation between blood viscosity and the development of atherosclerosis has been studied extensively, particularly in clinical research\(^5-10\). It has been demonstrated that an elevated blood viscosity is a predictor of the development of cardiovascular disease\(^10\). It is a well known fact, that plaque development near the carotid bifurcation occurs particularly in regions with recirculation, i.e. where the WSS oscillates\(^11,12\).

The goal of this study was to investigate the influence of hematocrit (Hct) levels, plasma viscosity, the flow rate and the vessel diameter on the WSR, WSS and on the recirculation regions. Because plaque development is related to regions where the WSS oscillates, special attention was given to the size and the amplitude of these oscillations. We simulated the flow through a model of a carotid artery bifurcation by means of the Finite Element Method (FEM). We used a well-tested model, the Carreau-Yasuda model, for non-Newtonian viscosity and varied Hct within ranges, which were obtained from a group of 49 healthy volunteers (Hct range: 0.346-0.506)\(^2,7\). In addition, the flow, the plasma viscosity and the diameter of the vessels were varied within realistic ranges. Also, MRI acquisitions were obtained in these young volunteers to obtain realistic flow rates during a cardiac cycle.

7.2 Materials and Methods

7.2.1 Materials

This study was based on in-vitro measurements using a carotid artery bifurcation model, and on in-vivo measurements in a group of 20 healthy young volunteers and 29 healthy elderly volunteers.

The phantom model was constructed of polymethyl methacrylate (PMMA) and had an inflow diameter of 8 mm, outflow diameters of 5.6 and 4.6 mm, for the internal carotid and external carotid arteries, respectively. MR examinations of the phantom were performed on a 1.5 T scanner (Gyroscan NT; Philips Medical Systems, Best, the Netherlands) using a standard knee coil. A phase contrast time-of-flight MR Angiographic acquisition protocol was applied without contrast agent. The acquisition parameters for the bifurcation phantom were as follows: 100 slices with slice thickness of 1 mm without gaps, TE/TR 6.8/21 ms, field-of-view (FOV) 150 mm and scan matrix of 512x512 pixels.

To obtain realistic flow rates and blood viscosities, in-vivo measurements were carried out in a group of 20 healthy young volunteers, 10 males and 10 females (average age 26.7 years, std.dev. 7.1). In these individuals the blood flow through the common carotid artery
was assessed with velocity encoded MRI; in addition, a blood sample was taken. The measurements were performed three times: at baseline, a first follow-up after one week and the second follow-up after 3 to 4 weeks. In addition, in vivo measurements were carried out in a group of 29 healthy elderly individuals (average age 74.6 years, stdev 5.1). Time-dependent blood flow was measured with a standard head coil. At the inflow position in the common carotid artery, the flow was assessed in a plane perpendicular to the major flow direction. Velocity encoded data was obtained by means of a gradient echo phase contrast imaging procedure. Triggering was applied during the acquisition and the cardiac cycle was subdivided into 16 equidistant phases. The imaging parameters were: TE/TR 11.2/18.44 ms, flip angle 15 degrees, slice thickness 2 mm, FOV 250 mm, scan matrix 256x256 and velocity sensitivity 100 cm/s. The number of signal averages was one. The scan time was dependent upon the heart rate, being 3 minutes at 60 beats/min. Hematocrit (Hct) is a measure for the amount of red cells in the blood. Hct was measured by a Coulter micro div II (Beckmann) apparatus. Blood viscosity was assessed with a Brookfield digital viscometer (model DVII+CP). This viscometer measures blood viscosity in a reliable manner at shear rates between 375 s⁻¹ and 750 s⁻¹. Finally, plasma viscosity was measured with an Oswald viscometer. Both viscometers were kept at a constant temperature of 37 degrees Celsius during the measurements. All samples were measured twice. In the following paragraphs the analytical steps are described in further detail.

7.2 Methods

7.2.2 Geometry assessment and mesh generation

The geometry of the acquired carotid bifurcation was segmented from the MR Angiographic data set (Fig. 1a) of the carotid bifurcation phantom using the analytical software package MRA-CMS. In brief, the segmentation procedure is based on the following principles. The user only needs to define a start- and endpoint in the 3D data space. This is facilitated by the 3D viewing capabilities of the MRA-CMS package. A 3D pathline is then automatically detected through the vessel segment connecting these points. In the second phase, the actual vessel segmentation process takes place based on the detected pathline. This segmentation is based on knowledge of the acquisition protocol and uses a deformable model of a vessel, which is deformed to fit the actual vessel wall. Each segmented vessel is expressed as a stack of cross sections, while a bifurcation is described by three vessel segments each consisting of a stack of cross sections (Fig. 1b). Figure 1c illustrates as an example the locations where the velocity profiles are measured. To be able to simulate the region between measured in- and outflow cross sections, the segmented image is cut off at these positions. The cross sections of the MRA-CMS-geometry were transformed to rectangles with the same spatial distribution as the rectangles at the surface of the mesh. A solver for linear elasticity was applied to transform the standard mesh (Fig. 1d). The Young's modulus E was set at a value of 100, while a small value was selected for the Poisson ratio $\nu = 1.0 \times 10^{-4}$ to allow for independent motion of the mesh in each coordinate direction. The standard mesh was thus transformed until it matched the MRA-CMS data set (Fig. 1e). To be able to study the effects of changes in vessel sizes due to changes in the diameter, this mesh was minified linearly by a factor of 0.9, i.e. all diameter sizes were reduced by a factor of 0.9 (Fig. 1f). Each mesh consisted of 9216 elements with 77669 nodal points.
7.2.3 Differential equations and method of solving

In this study we used the finite element modeling approach for solving the time-dependent Navier Stokes equations and the continuity equation,

\[ \frac{\partial \mathbf{v}}{\partial t} + (\mathbf{v} \cdot \nabla) \mathbf{v} = -\nabla p + \nabla \cdot \eta \nabla \mathbf{v} \]
\[ \nabla \cdot \mathbf{v} = 0, \]

where \( \mathbf{v} \) is the velocity vector, \( p \) is the pressure and \( \eta \) the kinematic viscosity. The elements were Crouzeix-Raviart type elements with 27 nodes, with a quadratic approximation for the three velocity components in each node. Both the pressure and the pressure gradient are defined at the centroid of each element. The package SEPRAN\textsuperscript{17} was used to generate the mesh and to build and solve the system of equations.

![Figure 1. A, MRA image; B, segmented image; C, position of velocity measurement; D, standard mesh; E, matched mesh; F, reduced diameter](image_url)

In this study only shear thinning properties of blood flow were taken into account; viscoelastic effects were not included. The calculations were performed on the TERAS
supercomputer at SARA, Computing and Networking Services, Amsterdam, the Netherlands. TERAS is a 1024-CPU system consisting of two 512-CPU SGI Origin 3800 systems (Silicon Graphics, California).

### 7.2.4 Boundary conditions
The velocity encoded MRI data were analyzed by means of the FLOW analytical software package (Medis medical imaging systems, Leiden, the Netherlands). FLOW allows the quantification of the flow versus time and the corresponding velocity profiles. The package FLOW presents the velocity distributions over the cross section of the vessel in several time slices during the cardiac cycle. Integration of the velocity profile over the cross section of the vessel $\Omega$ yields the variation of the flow through the vessel as a function of time $\text{flow}_{\text{MR}}(t)$. $\text{flow}_{\text{MR}}(t)$ was measured in the common carotid artery; these data were Fourier transformed, and the first 20 Fourier coefficients were used as input in the FEM calculations. In this study the velocity profile for the inflow was modeled by a Womersley profile for the measured flow rate. The Womersley profile was taken to avoid further investigations in the effects caused by smoothing of the velocity profile and in systematic MR-errors as for instance the partial volume effect. There were no constraints defined for the outflow, so that the flow through the bifurcation was only determined by inflow, geometry and friction.

### 7.2.5 Viscosity
Blood viscosity in humans is non-Newtonian. With increasing shear rate, the viscosity decreases. These shear thinning properties can be modeled by the Carreau –Yasuda model (CY model):

$$\eta = \eta_\infty + (\eta_0 - \eta_\infty) \left[1 + (\lambda_{cy} \gamma)^\alpha\right]^{(n-1)/\alpha}$$

where $\eta$ is the viscosity for shear rate $\gamma$, $\eta_\infty$ is the viscosity for infinite shear rate and $\eta_0$ the plasma viscosity at shear rate zero, $\lambda_{cy}$, $n$ and $\alpha$ are fitting parameters. For a well tested blood mimicking fluid, the KSCN-X solution, these parameters have the following values: $\eta_0=22$ mPa.s; $\eta_\infty=2.2$ mPa.s; $a=0.644$; $n=0.392$; $\lambda_{cy}=0.110$ s. Gijsen used this blood mimicking fluid to demonstrate that viscoelastic effects are not important under these flow conditions.

The viscosity in humans, however, can differ between individuals, among others due to differences in hematocrit levels. Matrai has demonstrated that the viscosity increases exponentially with increasing Hct. The method proposed by Matrai is widely accepted, and used to correct for the variations in blood viscosity caused by a variation in hematocrit. Since the power-law index $n$ in the CY-model is variable and $n$ is placed in the exponent, we propose to replace $n$ by Hct. To substantiate this adaptation, the results of the adapted CY model were compared with the measured viscosities.

### 7.2.6 Method of comparison between studies
As a first step, a comparison between our WSS values and the results described in the literature was carried out, starting with published ultrasound measurements in the common carotid artery. For this purpose, we addressed differences between ultrasound measurements described by Samijo et al., echo Doppler measurements by Gnasso et al. and MRI-measurements with FEM-simulations discussed in this article. For this comparison, the Hagen-Poiseuille formula was used, which is applicable for steady fully-developed flow in a circular pipe (parabolic velocity profile), 102
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\[ Q = \frac{\max \pi D^2}{8} \text{ and } \nu_{\text{mean}} = 0.5 \nu_{\max}, \]  

(4)

where \( Q \) is the flow rate, \( \nu_{\max} \) is the maximum flow velocity in the cross section and \( D \) is the diameter.

Assuming this parabolic velocity profile, the WSS can be calculated through eq 4. This was done by Gnasso et al.\textsuperscript{25} with the following result:

\[ \text{WSS} = 4\mu \frac{\nu_{\max}}{D}, \]  

(5)

where \( \mu \) is the Newtonian viscosity, \( \nu_{\max} \) is the maximum blood velocity measured in the center of the lumen, and \( D \) the diameter of the lumen.

### 7.2.7 Width of Systolic peaks

The width of the systolic peak (expressed in time slices) was calculated as well, and the widths of systolic peaks for the WSS and flow rates were compared. The usual Full Width Half Maximum was not suitable for every time series under study. Therefore, we introduce the Full Width Quarter Maximum (FW3QM), being the width of the peak where the height of the systolic peak was at 75% of its maximum.

### 7.2.8 Amplitude of WSR oscillations in recirculation regions

Plaque development is related to recirculation regions where the WSS is oscillating\textsuperscript{11,12,27,30}. We looked further into the amplitude of these oscillations where the velocity vector has opposing directions during the cardiac cycle. We investigated the amplitude of oscillations in these regions in our carotid bifurcation in relation to Hct, plasma viscosity, flow rate and vessel diameter. The FEM-package is capable of calculating the absolute values of the WSR at the edge of the mesh; the WSR vector, however, is not available. Therefore, we have taken the following approach: for each nodal point the closest nodal point which is not at the edge was used to access the velocity vector \( v = (v_1, v_2, v_3) \). Taking these vectors into consideration, the amplitude of velocity oscillations was taken at the location where the difference between back– and forward flow during the cardiac cycle was largest. The amplitude (amp) is then defined as follows:

\[ \text{Amp} = \sqrt{\left( v_{1\text{pos}} - v_{1\text{neg}} \right)^2 + \left( v_{2\text{pos}} - v_{2\text{neg}} \right)^2 + \left( v_{3\text{pos}} - v_{3\text{neg}} \right)^2}, \]  

(6)

where \( v_{\text{pos}} = (v_{1\text{pos}}, v_{2\text{pos}}, v_{3\text{pos}}) \) is the vector in the main flow direction and \( v_{\text{neg}} = (v_{1\text{neg}}, v_{2\text{neg}}, v_{3\text{neg}}) \) is the vector in the direction opposite to the main flow direction. The largest area of oscillation is presented and, in addition, integrated over time, this is called the ROAIT. The fraction of time when backflow is observed is called the NEGDIR.

### 7.2.9 Protocol

In this article the effects of three Hct values, two flow curves, two plasma viscosities and two diameters are compared. Data assessed from the volunteers with the lowest, the average and the highest Hct, were used in this article. Flow(t) profiles in the common carotid artery were measured by velocity encoded MRI. Flow curves from two volunteers were selected for further analysis. The flow curve measured in the volunteer with the lowest Hct (volunteer I, female) is denoted Flow(HctMin) and the curve assessed in the volunteer with the highest Hct (volunteer III, male) is denoted Flow(HctMaxmeas).
To be able to study the effects on the WSR and WSS caused by the flow rate only, it is important to compare two flow curves with the same shape. Therefore, we normalized the two flow curves in the following manner. The height of the systolic peaks is used to determine a multiplication factor for Flow(HctMin). The measured flow curve Flow(HctMaxmeas) is adapted, which gives Flow(HctMax) is calculated by:

\[
\text{Flow(HctMax)} = \left\{ \frac{\text{max}[\text{Flow(HctMaxmeas)]}}{\text{max}[\text{Flow(HctMin)]}} \right\} \times \text{Flow(HctMaxmeas)}
\]

(see also Fig. 2). To study the effects on the WSR and WSS caused by Hct, we proposed earlier in this manuscript to replace \( n \) in the Carreau-Yasuda model (Eq. 3) by Hct. The WSR and WSS were calculated for the lowest, an average and the highest Hct measured in the group of healthy volunteers.

To study the effects on the WSR and WSS caused by a difference in plasma viscosity, two plasma viscosity values were used in the Carreau-Yasuda model prior to simulation. Based on the KSCN-X solution \( \eta_\infty = 2.2 \text{ mPa.s} \) was taken and based on measurements of plasma viscosity \( \eta_\infty = 1.1 \text{ mPa.s} \) was used\(^{24}\).

To study the effects on the WSR and WSS caused by variations in diameter, simulations for two diameters were carried out: one for a mesh with an inflow radius of 3.876 mm and one for an inflow radius of 3.488 mm, being 90% of the first diameter.

For inter-study comparisons in this article we used Eq. 4 and 5. The method proposed by Gnasso is easily applicable and widely used and accepted\(^{25}\).

We investigated the size of the oscillating regions, and the amplitude of these oscillations, in relation to Hct, plasma viscosity, flow rate and vessel diameter. In addition, we introduced parameters to quantify oscillations in the whole bifurcation, the ROAIT and the NEGDIR. These parameters are closely related to parameters which quantify the oscillations locally and can be correlated to the presence of plaques\(^{27,30}\).
Figure 3. A, The Carreau-Yasuda (CY) model for the parameters fitted to the KSCN_X solution. B, The CY-model for $n=0.346$, $n=0.432$, $n=0.506$ and the measured viscosities for Hct =0.346 (volunteer I), Hct=0.432 (volunteer II), and Hct=0.506 (volunteer III). C, The CY-model for average Hct=$n=0.356$, 0.426 and 0.495. Note that for visualization the shear rates are shifted for Hct=0.356 to the right and for 0.426 to the left. D, The CY-model for the parameters fitted to the KSCN_X solution with $n=0.346$, $n=0.432$, $n=0.506$ (thick lines) and for $n_{\infty}=1.1mPas$ (thin lines).

7.3 Results

7.3.1 Whole blood viscosity for high plasma viscosity

From the (in total 89) blood samples, the samples with the lowest, the average and the highest Hct were selected. These Hct values in percentage were found to be 0.346, 0.432 and 0.506 in volunteers I, II and III, respectively. Hct values were directly inserted in the CY model with the power law index $n$ replaced by Hct (Fig. 3, Eq. 3). All the other parameters were kept equal to those for the blood mimicking fluid, the KSCN-X solution, being: $\eta_0=22 mPas$; $\eta_\infty=2.2mPa.s$; $a=0.644$; $n=0.392$; $\lambda_{cy}=0.110 s.2$

In 89 blood samples from the 20 healthy young volunteers (each volunteer was measured 3 times) and from the group of 29 healthy elderly volunteers, viscosities were measured at the shear rates of 375, 450 and 750 1/s. The blood samples were grouped by the value of Hct as follows: group 1: Hct $\leq 0.376$; group 2: Hct $\geq 0.402$ and Hct $\leq 0.462$; group 3: Hct $\geq 0.486$. The average Hct level and the number of samples within each bin were as
follows: Group 1 (0.356, N=17); Group 2 (0.426, N=51); and Group 3 (0.495, N=4), respectively. Figure 3 demonstrates that when n is replaced by Hct in Eq. 3, the measured viscosities show a good agreement with the calculated viscosities.

The calculations were repeated with half the plasma viscosity as found for the KSCN-X solution. The differences in viscosity compared to \( n_\infty = 2.2 \text{ mPas} \) are shown in Figure 3D. The measured plasma viscosities were 1.09 ± 0.01, 1.11 ± 0.01, and 1.04 ± 0.006 mPas for volunteer I, II and III, respectively. Samijo measured an average plasma viscosity of 1.11 mPas both in healthy young males and females.

7.3.2 WSR and WSS for high plasma viscosity
After applying FEM-simulations for the flow curves Flow(HctMin), and Flow(HctMax), a region in the common carotid artery was selected for the assessment of the WSR and WSS (Fig. 4). In Table 1 the WSR and WSS during Peak Systole (PS), during diastole (DS) and averaged over the cardiac cycle (M) for the flow curves Flow(HctMin) and Flow(HctMax) are presented. For comparison purposes the results for the volunteers measured by Samijo and Gnasso are also presented in this table. Samijo measured with ultrasound in the common carotid artery for males a peak systolic blood velocity (PSV) of 104.5 cm/s and averaged over the cardiac cycle (MV) 32.0 cm/s. Assuming a parabolic velocity profile (Eq. 4) this gives for the peak-systolic flow \( Q_{ps} = 24.7 \pm 4.7 \text{ ml/s} \) and for the mean flow \( Q_m = 7.5 \pm 1.1 \). For females, these results are: PSV=81.7 cm/s and MV=26.7 cm/s. This gives \( Q_{ps} = 19.3 \pm 2.8 \text{ ml/s} \) and \( Q_m = 6.3 \pm 1.1 \text{ ml/s} \). Gnasso measured also in the common carotid artery with echo Doppler the velocity of the blood, being 97.1 cm/s during systole (Vps) and 30.2 cm/s on average (VM). Under the assumption of a parabolic velocity profile and using the diameter in the calculations (Eq. 4) \( Q_{ps} = 22.9 \text{ ml/s} \) and \( Q_m = 7.1 \text{ ml/s} \). Our Flow(HctMin) curve gives \( Q_{ps} = 15.1 \text{ ml/s} \) and \( Q_m = 5.71 \text{ ml/s} \). The Flow(HctMax) curve gives \( Q_{ps} = 20.5 \) and \( Q_m = 5.62 \text{ ml/s} \). Samijo’s blood velocity measurements are combined with eq 4, our diameter, which is 7.75 mm, and the calculated viscosity at shear.
Figure 6. Viscosity for the Peak WSS (A) and MWSS (B), Peak-WSR (C) with Peak-WSS (E) and Mean-WSR (D) with Mean-WSS (F) during the cardiac cycle for flow curve Flow(HctMin) and Flow(HctMax). The flow curves are scaled at the highest WSS for the lowest flow curve Flow(HctMin) using formula 7. The scaled flow curves are shown in figure C, D, E and F.
rate of 225 s$^{-1}$ with an average Hct, which is 5.08 mPas. The results from these calculations are indicated with Samijo*.

After simulation the Peak WSR in the bifurcation during the peak systole was selected (PWSR$$_{PS}$$), and the Peak WSR averaged over the cardiac cycle (PWSR$$_{M}$$) was calculated. In addition, the Mean WSR was assessed at peak systole (MWSR$$_{PS}$$) and averaged over the cardiac cycle (MWSR$$_{M}$$). These parameters were calculated for three viscosity curves (Fig. 3), for two flow curves (Fig. 2) used as inflow, and for two vessel diameters (Fig. 1e, 1f). The PWSR was located between the internal and external branch of the carotid bifurcation.

In Figure 5 (p 113) an example of the WSR distribution for two time slices, one during peak-systole and one during diastole is given. It is clear that during systole the WSS is higher compared to diastole.

<table>
<thead>
<tr>
<th>Source</th>
<th>WSR$$_{PS}$$ (s$^{-1}$)</th>
<th>WSS$$_{PS}$$ (Pa)</th>
<th>WSR$$_{DS}$$ (s$^{-1}$)</th>
<th>WSS$$_{DS}$$ (Pa)</th>
<th>WSR$$_{M}$$ (s$^{-1}$)</th>
<th>WSS$$_{M}$$ (Pa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEM-Flow (HctMin)</td>
<td>570.9</td>
<td>2.64</td>
<td>41.5</td>
<td>0.38</td>
<td>92.3</td>
<td>0.62</td>
</tr>
<tr>
<td>FEM-Flow (HctMax)</td>
<td>834.7</td>
<td>3.52</td>
<td>60.3</td>
<td>0.50</td>
<td>136.9</td>
<td>0.83</td>
</tr>
<tr>
<td>Samijo-males</td>
<td>1338</td>
<td>4.3</td>
<td>-</td>
<td>-</td>
<td>414</td>
<td>1.3</td>
</tr>
<tr>
<td>Samijo-*males</td>
<td>-</td>
<td>2.75</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.84</td>
</tr>
<tr>
<td>Samijo-females</td>
<td>1074</td>
<td>3.3</td>
<td>-</td>
<td>-</td>
<td>379</td>
<td>1.2</td>
</tr>
<tr>
<td>Samijo-*females</td>
<td>-</td>
<td>2.15</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.70</td>
</tr>
<tr>
<td>Gnasso</td>
<td>-</td>
<td>2.95</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1.2</td>
</tr>
</tbody>
</table>

Table 1. WSR and WSS for FEM simulations for two flow curves compared to measurements with ultrasound$^{24}$ and echo-Doppler$^{25}$. WSR and WSS are presented for Peak Systole (PS), Diastole (DS) and averaged over the cardiac cycle (M). Also a combination is made between Equation 4 and 5, ultrasound-measurements by Samijo, our diameter (7.75 mm), and the calculated viscosity at shear rate of 225 s$^{-1}$ used by Gnasso for an average Hct (5.08 mPas). This gives the results indicated with Samijo*.

![Graph A](image1.png)

**A.**

![Graph B](image2.png)

**B.**

**Figure 7.** Viscosity for the Peak WSS (A) and MWSS (B), during the cardiac cycle for flow curve Flow(Hctmin) and Flow(Hctmax). The flow curves are scaled at the highest WSS for the lowest flow curve Flow(HctMin) using formula 7.

The WSS is always low at the outer walls on the left and right hand side in the region of the bifurcation. In the pictures on the left in Figure 6 the Peak WSR, Peak WSS and the
related viscosities during the cardiac cycle are presented for different Hct-values and flow values. In the pictures shown at the right hand side in Figure 6, the MWSR, MWSS and the related viscosity are shown. It can be observed that the viscosity for high flow is much more sensitive to Hct than the viscosity for low flow (Fig. 6A, 6B).

An increase in Hct leads to a decrease in WSR and an increase in WSS. The viscosity increases with Hct. These characteristics are observed for both flow curves. Scaled flow curves are shown in the same figure as WSR and WSS so that the shapes can be compared visually. It can be observed clearly that Peak WSS is very sensitive to flow increases. The Mean WSS is much less sensitive to flow increases. In Figure 8A and B the reactions on flow variance and diameter change are shown. According to Equations 4 and 5, the WSS has a linear relation with the flow. Flow curve Flow(HctMax) is assessed by a multiplication of flow curve Flow(HctMin) with 1.36. Figure 6G shows that the PWSS increases much more than proportional to flow. For a flow increase by a factor of 1.36, the average increase in PWSS is 1.88. Also the MWSS increases more with the flow than suggested by equations 4 and 5. The average increase for the MWSS is 1.68. High Hct makes WSS a little less sensitive to flow increase.

According to Equation 5, a decrease in diameter has an increasing effect on the WSS. In healthy volunteers the carotids of elderly individuals have shown to have a smaller vessel size compared to those of young individuals. Therefore, we wanted to investigate the effect of diameter reduction. The diameter was decreased to 90% of its original size: the larger inflow cross section was 0.47 cm², for the simulations with the small diameter it is 0.38 cm². The diameter decrease is expected to give an increase in the WSS by a factor of 1.37. For the PWSS averaged over the cardiac cycle the WSS-increase is larger than expected: it is 1.57. The MWSS gives a lower increase 1.25. Hct has little influence on the effects of diameter reduction.

Remarkable is that for diameter reduction the systolic peak shifts to the left with flow increase (Fig 8B and 10B). Although Eq 5 predicts the same influence for diameter reduction and flow increase our simulations show much bigger effects for flow increase (Fig. 8A and 8B).

We also investigated the responses to increases in Hct values. Responses were calculated for the increases from Hct=0.346 to Hct=0.432 and from Hct=0.432 to Hct=0.506 as follows. For the investigated flow rates and diameters the responses were approximately constant. The WSR reduces and the WSS increases. On average the responses were: For Peak systole PWSR=0.97, PWSS=1.07, MWSR=0.95 and MWSS=1.02. Averaged over the cardiac cycle PWSR=0.93, PWSS=1.05, MWSR=0.95 and MWSS=1.09, respectively.

### 7.3.3 WSR and WSS for low plasma viscosity

The calculations were repeated with half $\eta_\infty$ (which is called for simplicity half the plasma viscosity) as found for the KSCN-X solution. In Figure 9 the PWSS and MWSS for Flow(HctMin) and Flow(HctMax) for low plasma viscosity and the flow curves themselves are shown. Visual inspection shows that the PWSS for low plasma viscosity during systole is more dependent on Hct than the PWSS for high plasma viscosity (see also Figure 6). For MWSS and low plasma viscosity the effect of flow increase from Flow(HctMin) to Flow(HctMax) is sometimes even smaller than the effect of Hct. Lower plasma viscosity leads to lower WSS for all Hct’s and parameters which were studied. In Figure 10A and 10B the reactions on diameter and flow variance are shown. As mentioned the multiplication factor for flow curve Flow(HctMin) to assess flow curve Flow(HctMax) = 1.36. As shown in Figure 10A the PWSS increases more than
proportional to flow, the average increase is 1.76. Also the MWSS increases more with the flow than can be expected for fully developed flow, the average increase is 1.64. The diameter decrease is expected to give an increase in the WSS of 1.37. For the Peak-WSS the WSS-increase is larger compared to Eq. 5, for peak systole it is 1.51. MWSS gives a lower increase, the average is 1.26. High Hct decreases influence of diameter reduction.

**Figure 8A.** Ratios of the WSS for high plasma viscosity caused by flow increase. Ratios are calculated for (parameter after action) / (parameter before action). FILD=Flow increase for the large diameter; FISD=Flow increase for the small diameter.

**Figure 8B.** Ratios in WSS for high plasma viscosity caused by diameter decrease. Ratios are calculated for (parameter after action) / (parameter before action). DDLF=Diameter decrease for the low flow; DDHF=Diameter decrease for the high flow.
Figure 9. The Peak and Mean WSS during the cardiac cycle for flow curves Flow(HctMin) and Flow(HctMax) for the low plasma viscosity. Scaled flow curves are indicated with *. The effects of Hct increase are approximately equal for Hct incr.1 and Hct incr.2. Low plasma viscosity shows stronger reactions than high plasma viscosity. The responses on higher Hct are approximately constant for all investigated flow and diameters. The WSR reduces and the WSS increases. For Peak systole PWSR=0.97, PWSS=1.14, MWSR=0.91 and MWSS=1.12. Averaged over the cardiac cycle PWSR=0.94, PWSS=1.17, MWSR=0.88 and MWSS=1.12.

Plasma viscosity has a large influence on the WSS. This is to be expected, since plasma viscosity changes the Reynolds number and therefore influences the Womersley parameter. For the MWSS the simulations resulted in differences from 9\% (MWSS_{M}, low flow, large diameter) to 27\% (MWSS_{PS}, high flow, small diameter) and for the PWSS from 22\% (PWSS_{M}, low flow, large diameter) up to 43\% (PWSS_{PS}, high flow, large diameter).
small diameter). Hct also influences the reactions rising from plasma viscosity changes. A low Hct increases the differences between high and low plasma viscosity.

**Figure 10A.** Ratios of the WSS for low plasma viscosity caused by flow increase. Ratios are calculated for (parameter after action) / (parameter before action). FILD=Flow increase for the large diameter; FISD=Flow increase for the small diameter.

**Figure 10B.** Ratios in WSS for low plasma viscosity caused by diameter decrease. Ratios are calculated for (parameter after action) / (parameter before action). DDLF=Diameter decrease for the low flow; DDHF=Diameter decrease for the high flow.
Figure 5. WSR for peak systole (A) and mid diastole (B) for flow curve Flow(HctMin) (see fig 2.), low plasma viscosity (see paragraph low plasma viscosity) and Hct=0.506. Note that the first and last elements for in- and outflow (lowest and highest positions in the figure), are colored red and are not used in the calculations of WSR and WSS.

7.3.4 Width of Systolic peaks
For all simulations the FW3QM (the amount of time slices that the WSS is above 0.75 times the amplitude) is given for the flow, the PWSS and MWSS in Fig 11. When for low flow (Flow(HctMin)) the PWSS-width is compared to the width of the flow curve, the width for the WSS is almost twice as wide for the PWSS. For the high flow (Flow(HctMax)) the systolic peak starts at approximately the same time as for the flow curve. For the low flow there is a delay. The MWSS shows some opposing behavior. For the low flow the width is smaller compared to the width of the systolic peak for the flow curves and increases a little bit with decreasing plasma viscosity. The effect of flow increase is larger than for PWSS. For the MWSS the systolic peak starts sooner than the peak of the flow curve. It is remarkable that Hct has an increasing effect on the peak width for the large diameter and a decreasing effect for the small diameter.

7.3.5 Amplitude of WSR oscillations in recirculation regions
In Table 2 the amplitude of oscillations are shown together with the location of the maximum and the time slice where this maximum is observed. It can be observed that high flow gives largest oscillation amplitude. It is seen that increasing Hct results mostly in a decreasing amplitude of WSR oscillations. In Table 2a the effects of an increasing flow rate, a decreasing diameter and a decreasing plasma viscosity are presented. A decreasing plasma viscosity and an increasing flow seem to give an increase of the amplitude of the oscillations. Furthermore can be observed that for high flow and decreasing diameter, the differences in plasma viscosity have much effect on the amplitude of the oscillations. Table 2a shows clearly that diameter decrease has less effect on the amplitude of oscillation when Hct increases. For low plasma viscosity, high Hct gives even a decrease in the amplitude of oscillation, when diameter decreases. The largest effect on the amplitude of oscillation however is caused by the change in flow rate in the vessel with the large diameter. In summary: The amplitude of oscillations is very dependent on flow, and less on diameter. The positions where the highest amplitudes are found are mostly at the edge of the recirculation regions.
Figure 11. The Full Width Quarter Maximum for the systolic peak (FW3QM). The black line at y=1 gives the FW3QM for the flow curve. The bars positioned under y=3 give the width of the systolic peaks for the large diameter. Above y=3 the FW3QM for the small diameter are given. A, gives the FW3QM for the PWSS, B, for the MWSS. Note that the presented x-axis in this figure is only 0.28% of the cardiac cycle.
### Table 2. The amplitude of oscillations near the vessel wall according to equation 7. LF=Flow (HctMin), HF =Flow(HctMax). The letter behind the amplitude indicates a color in Figure 12. It gives the position where the highest oscillation amplitude is found, R=red; Y=yellow; G=green; C=cyan; B=blue, M=magenta. The number behind the color indicates in which time slice the highest amplitude is found.

<table>
<thead>
<tr>
<th>Action</th>
<th>Hct</th>
<th>hpv</th>
<th>lpv</th>
<th>Hct</th>
<th>hpv</th>
<th>lpv</th>
<th>Hct</th>
<th>hpv</th>
<th>lpv</th>
</tr>
</thead>
<tbody>
<tr>
<td>flow increase BD</td>
<td>0.346</td>
<td>1.98</td>
<td>1.44</td>
<td>0.432</td>
<td>1.79</td>
<td>2.67</td>
<td>0.506</td>
<td>2.57</td>
<td>3.80</td>
</tr>
<tr>
<td>flow increase SD</td>
<td>2.27</td>
<td>2.08</td>
<td>1.72</td>
<td>2.20</td>
<td>1.83</td>
<td>1.91</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>diam decrease low flow</td>
<td>1.33</td>
<td>1.35</td>
<td>1.41</td>
<td>1.33</td>
<td>1.63</td>
<td>1.72</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>diam decrease high flow</td>
<td></td>
<td>1.52</td>
<td>1.95</td>
<td>1.36</td>
<td>1.10</td>
<td></td>
<td>1.16</td>
<td>0.86</td>
<td></td>
</tr>
<tr>
<td>pl visc decrease BD</td>
<td>1.90</td>
<td>0.86</td>
<td>1.13</td>
<td>1.69</td>
<td>1.21</td>
<td>1.78</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pl visc decrease SD</td>
<td>1.21</td>
<td>1.11</td>
<td>1.07</td>
<td>1.37</td>
<td>1.27</td>
<td>1.32</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 2A. The ratio of (parameter after the action) / (parameter before action) between the amplitude of oscillation for flow increase and diameter decrease, where hpv is high plasma viscosity and lpv is low plasma viscosity. The ratio is: (oscillation amplitude after the action) / (oscillation amplitude before the action). The action is plasma viscosity decrease, where BD is Big Diameter and SD is Small Diameter.
Figure 12. The direction of the velocity vector at the nodal points nearest to the vessel wall. The length of the lines indicate the size of the vector, green lines indicate a velocity vector in the direction of the major flow, red lines indicate recirculation. The largest recirculation region during the cardiac cycle (in red), for the big diameter (A) low flow, high plasma viscosity and Hct=0.346 and for the small diameter (B) high flow, low plasma viscosity and Hct=0.356. The colored dots refer to the positions where the highest oscillation amplitudes are found (see also Table 2).

7.3.6 Size of recirculation regions
We investigated the size of the recirculation regions in our carotid bifurcation in relation to Hct, plasma viscosity, flow-rate and vessel diameter. In Figure 12 the large and small vessel diameter with the maximum oscillation area are shown. The green lines indicate forward flow, the red lines backward flow. The length of the lines is a measure for the size of the velocity vector in the nodal points nearest to the surface nodal point. At the surface itself the blood velocity was zero (no-slip boundary conditions).

The size of the regions where flow in negative direction was observed is depicted in Figure 13 on the y-axis. On the x-axis the timeframes where recirculation was observed are shown. To be able to compare the bifurcation with the large and small diameters, the region sizes where back flow was observed, were divided by the total surface area. This is called the relative oscillation area. The total surface area for the bifurcation with the large diameter was 12.64 cm², for the small diameter it was 11.19 cm². Figure 13 shows that the highest Hct gives the smallest oscillating regions. Lower plasma viscosity increases mainly the size of the regions and has little effect on duration when back flow is observed. Lowering Hct and plasma viscosity has most influence on the size of the back flow region in the secondary peak.

For high flow the region with backward flow is observed sooner and the secondary peak is bigger. Decreasing the diameter has little effect on the amplitude and time of the first recirculation region (both in space and in time), in the secondary peak region it has some effect on the region size.

To have an indication of the impact of the reversed flow, the relative oscillation area is integrated over time (ROAIT) In addition, the fraction of time that the WSS is pointing in the negative direction is calculated (NEGDIR). The results are presented in Table 3. It can be observed that high viscosity and low flow decreases ROAIT and NEGDIR. The diameter does not have much effect on these parameters.
Figure 13 A, The size of the regions with backward flow divided by the total surface of the vessel wall. The upper two figures (13a.1 and 13a.2) are for the large diameter, the lowest two figures (13a.3 and 13a.4) are for the small diameter. Figures 13a.1 and 13a.3 are for low flow, figure 13a.2 and 13a.4 are for high flow. Red gives the region for Hct=0.346, green Hct=0.432; blue Hct=0.506. The full lines are for high plasma viscosity and the dashed lines are for low plasma viscosity. B, The size of the region with backward flow divided by the total surface of the vessel wall. An average is taken for the Hct’s. Cyan= low flow, large diameter; Blue= high flow, large diameter; Red= low flow small diameter; green = high flow small diameter. Full line = high plasma viscosity, dotted line is low plasma viscosity.
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Table 3. The relative oscillation area integrated over time / the fraction of time that flow in the negative direction is observed (in percentage).

<table>
<thead>
<tr>
<th>Hct</th>
<th>LF high pl.visc</th>
<th>LF low pl.visc</th>
<th>HF high pl visc</th>
<th>HF low pl visc</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.356</td>
<td>3.69 / 42</td>
<td>4.33 / 48</td>
<td>4.41 / 72</td>
<td>4.96 / 82</td>
</tr>
<tr>
<td>0.432</td>
<td>3.09 / 38</td>
<td>3.66 / 40</td>
<td>3.87 / 56</td>
<td>4.43 / 74</td>
</tr>
<tr>
<td>0.506</td>
<td>2.49 / 36</td>
<td>2.97 / 38</td>
<td>3.37 / 50</td>
<td>3.81 / 60</td>
</tr>
<tr>
<td>Diameter is 0.3488:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.356</td>
<td>4.07 / 44</td>
<td>4.75 / 46</td>
<td>4.78 / 74</td>
<td>5.29 / 84</td>
</tr>
<tr>
<td>0.432</td>
<td>3.45 / 40</td>
<td>4.03 / 38</td>
<td>4.23 / 62</td>
<td>4.82 / 74</td>
</tr>
<tr>
<td>0.506</td>
<td>2.84 / 38</td>
<td>3.39 / 38</td>
<td>3.69 / 50</td>
<td>4.22 / 70</td>
</tr>
</tbody>
</table>

7.4 Discussion

We propose in this study a whole blood viscosity modeling where viscosity is dependent on Hct in an exponential manner. Much literature is available about the measurements and modeling of blood viscosity. Some mention a linear relation between Hct and viscosity under 45% Hct and faster above32. It has been shown by other investigators that the relationship between blood viscosity and Hct is well approximated by an exponential function20,33. However, when more aspects of the red cells, as for instance red cell aggregation and the internal viscosity of the red cells are taken into account, the modeling can be improved34,35. Furthermore there is discussion about inherent errors caused by the apparatus36,37. We are aware that our viscometer was not ideal for blood viscosity measurements. For a first approximation of shear thinning habits of the whole blood viscosity, the modified Carreau-Yasuda model has proven to give good results (Fig. 3B,3C).

Our WSR and WSS at the top of the bifurcation are rather large (WSS up to 30 Pa for Flow(HctMax), small diameter and Hct=0.506) compared to some measurements in the literature27. Zarins, however, reported PWSS measurements of 60 Pa at places where abrupt changes in geometry are observed28. Perhaps our large PWWS is caused by our geometry, which shows a sharp transition between internal and external carotid artery. When Fig 6,7 and 9 and are compared we observe a large influence of plasma viscosity in the PWSS and a significant contribution of plasma viscosity on the MWSS.

With increasing flow the WSR increases also. With increasing shear rate the viscosity decreases. Therefore the WSS, (being the product of the two), is formed by two counter-acting parts. Both for low and high plasma viscosity the peak- and mean WSS increases with Hct. The WSR is larger for low plasma viscosity and the WSS is lower. This differs up to 42% in the example in this article. This fact seems in contradiction because it is known that high WSS is healthy and we know also that low plasma viscosity is healthy. A combination of high flow and small diameter has a large effect on WSR and WSS. The diameters in this experiment were not as small as diameters measured by Samijo24. Our smallest diameter was 6.98 mm, Samijo’s diameter was 6.12 mm on average. However, when both plasma viscosity is low and the flow is high the WSS can rise above 40 Pa, which may cause endothelial injury29.
In Figure 6, 7 and 9 can be observed that increasing viscosity gives (caused by a high Hct or a high plasma viscosity) a low WSR and a high WSS. PWSS is more sensitive to flow increase than expected with Eq. 4 and 5. For the MWSS it is seen that, when the flow is increased the systolic peak of the MWSS series broadens and peak height increases slower than the peak height of the flow.

When systolic peak widths (in time) are observed, the PWSS peaks are broader than the peak width of the flow. The MWSS peak is smaller for the big diameter, and broader for the small diameter, compared to the broadness of the systolic peak of the flow profile. The systolic peak for the PWSS clearly showed a stronger increase in peak height and width, for both low and high plasma viscosity when the flow was increased, compared to the flow rate itself. For the MWSS this increase is not seen. For high flow the systolic peak of the MWSS seem to form a shoulder on the right side so that broadness increases. The amplitude of recirculation is very sensitive for the flow rate (Table 2). The position where the highest amplitude is found is not always the same. The oscillation amplitude for Flow(HctMax) is 44% up to 280% larger compared to the ones for Flow(HctMin). The difference in flow rate is only 36.5%. Other studies have investigated the effects of flow increase on the amplitude of oscillation. Moore saw that a flow increase by 300% gave rise to a decrease in the oscillation. Liepsch, however, mentioned that secondary flow becomes stronger with higher flow, which is in agreement with our results. He also investigated the change in flow rate ratio between the two branches in a bifurcation, which is a result of the higher resistance in the internal carotids artery due to recirculation. The recirculation amplitude is also rather sensitive to differences in viscosity and diameter. The position of the maximum oscillation varies but is always at the edge of the region where backflow is observed. Although we observe two outliers, in common it is observed that increasing flow, and decreasing plasma viscosity increases the amplitude of oscillation (Table 2 and 2a). In Figure 13 and Table 3 it can be observed that increasing flow leads to an increase in oscillation region. The consequence of viscosity increase is a decreasing oscillation region. The amplitude of Oscillation and the ROAIT in Table 3 is closely related to the oscillatory shear index (OSI) and the NEG index. OSI is an indication for oscillations in the shear direction calculated for the axially directed WSS according to the formula:

\[
\text{OSI} = \frac{|A_{\text{neg}}|}{|A_{\text{pos}}| + |A_{\text{neg}}|},
\]

where \(|A_{\text{neg}}|\) and \(|A_{\text{pos}}|\) are the areas under the shear stress versus time curve when shear is negative and positive respectively. NEGDIR is closely related to the NEG index, which gives the fraction of time that the WSS was in the negative direction.

\[
\text{NEG}=\frac{T_{\text{neg}}}{T},
\]

where \(T_{\text{neg}}\) is the time the WSS is in the negative direction and \(T\) is the total time, which is one cardiac cycle in this study. OSI and NEG are quantities, which are connected to a certain position. These quantities are not calculated for a whole vascular structure. Because NEG and OSI have such a strong correlation with plaques we would like to point out here that ROAIT and NEGDIR in this study suggest that plaque development is not much influenced by the diameter of the vessel but that flow increase and viscosity decrease give more pronounced recirculation and contribute in this manner to plaque development. This seems in contradiction to the fact that several studies have found a relation between elevated blood viscosity and atherosclerosis. For realistic investigations of recirculation it seems important to study non-Newtonian fluids instead of Newtonian fluids as is stated
by Moravec and Liepsch. In our model vessel distensibility and viscoelasticity are not taken into account. Perhaps this simplification can explain the contradictory results between medical studies and the calculations.

In Figure 8 and 10 is shown that flow increase has much more effect that diameter decrease. This is also seen in the oscillations and is in agreement with Moore and Liepsch.

In Table 1 our results for high plasma viscosity are compared with measurements from Samijo and Gnasso. The agreement between the results is good. About the comparison between the measured flow values with phase contrast MRI the following can be said: Seitz has shown that ultrasound measures lower flow values for the mean velocity and high flow values for the peak systolic velocity. Hoppe showed that Intravascular Doppler Ultrasound measured generally higher flow velocities compared to phase contrast MRI. This is also what seems to be the case for our measurements compared to Samijo and Gnasso.

Samijo measured with ultrasound several parameters. He compared diameter, mean velocity, peak systolic velocity, PWSR(t), MWSS(t), MWSS(t) and Hct in healthy male and female volunteers. The males had the highest values for all mentioned parameters and the differences were as follows: diameter (4%), mean velocity (17%), peak systolic velocity (22%), PWSR (20%), MWSS (23%), MWSS (12%). The differences in Hct, peak systolic velocity, mean velocity and MWSS where significant.

With the results of our study we can partly trace which parameters are the probable causes for the significant difference in PWSS between men and women. When Hct is higher, blood viscosity is higher, WSR is lower and WSS is higher. Men have a significant higher Hct (difference 11%). As a result of this we expect the WSR to be lower and the WSS to be higher in men. The high velocity in men is linearly related to the flow rate and gives a higher WSR. By using Table 2a and 3a we can compare the effects of flow increase combined with Hct increase. In our study we have an increase of 15% in Hct between Hct=0.432 and 0.506 and an increase in flow of 27%. This gives an increase in MWSR of 35%, in MWSS of 37%, in MWSS(t) of 49% and in MWSS(t) of 45%. All our increases are larger than mentioned by Samijo but results seem to be comparable. Samijo measured a higher WSR for men. From our experiments we can deduce that the high WSR in men is therefore most probably not caused by Hct but is dependent on the high blood velocity (which is equivalent to blood flow) for men.

7.5 Conclusions

Blood viscosity is measured at shear rates between 375, and 750 s\(^{-1}\). In this range, the Carreau-Yasuda model gives a good approximation of the viscosity for the blood of the volunteers when the power law index \(n\) is replaced by Hct.

For lower Hct the WSR is higher. The WSS, being the product of WSR and viscosity, decreases with decreasing Hct. It decreases also when plasma viscosity is lowered. When flow is increased, peak WSS seems to increase at a higher rate than the peak systolic flow. The mean WSS seems to increase at a lower rate than peak systolic flow. Plasma viscosity has a large influence on the WSS. When plasma viscosity is low MWSS increases less than flow. For low plasma viscosity the WSS is more dependent on Hct. High plasma viscosity gives high PWSS. Increasing the flow leads to a huge increase in the amplitude of oscillations in the recirculation region. The maximum amplitude of oscillations is almost always found at the edge of the recirculation region. Hct increase has a decreasing effect on
recirculation amplitude and region size and has to a smaller extent a decreasing influence on recirculation time. In common low plasma viscosity causes a large size and amplitude of oscillations.

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