Wall shear stress calculations using phase contrast MRI

Potters, W.V.

Citation for published version (APA):
Potters, W. V. (2015). Wall shear stress calculations using phase contrast MRI

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

UvA-DARE is a service provided by the library of the University of Amsterdam (http://dare.uva.nl)
Chapter 3

Volumetric arterial wall shear stress calculation based on cine phase contrast MRI

Wouter V. Potters
Pim van Ooij
Henk A. Marquering
Ed van Bavel
Aart J. Nederveen

Volumetric arterial wall shear stress calculation based on cine phase contrast MRI

doi: 10.1002/jmri.24560
3.1 Introduction

The effect of blood flow on the vascular endothelium has been proposed to be a critical determinant of vascular disease progression in atherosclerosis and aneurysms \(^1\) \(^2\). This effect is suggested to primarily relate to the local wall shear stress (WSS), i.e. the tangential force per surface area acting on the endothelial cells \(^3\). Both low and oscillating WSS patterns have been reported to correlate with atherosclerosis \(^4\)\(^-\)\(^7\) and aortic dilatation \(^8\)\(^-\)\(^9\), whereas high WSS was found in aortas with bicuspid valves \(^9\)\(^-\)\(^10\). High WSS is believed to be a stimulus for physiological remodeling of the blood vessel wall and for maintaining an atheroprotective phenotype \(^4\). In addition, spatial WSS gradients have been suggested to relate to intracranial aneurysm progression \(^2\) and rupture risk \(^11\), although an early warning sign for cardiovascular disease progression and acute events such as atherosclerotic plaque rupture and aneurysm rupture.

WSS can be estimated from temporal and spatial information on velocity direction and magnitude. Three-dimensional cine phase contrast magnetic resonance imaging (3D cine PC MRI) or 4D flow MRI, is currently the only method to noninvasively measure 3D velocity vector fields in a volume in vivo. WSS direction and magnitude can be obtained from spatial derivatives of these velocities on the vessel wall \(^12\).

Stalder et al. presented a method for calculation of WSS magnitude and direction using in vivo 3D cine PC MRI data, in which b-splines (piecewise polynomial functions) were applied for velocity field fitting \(^13\). However, their method was only applicable in 2D cross-sectional slices of the vessel geometry. Approaches in which the WSS vector is calculated at each wall position were presented by Boussel et al. in intracranial aneurysms \(^14\) and Bieging et al. in the ascending aorta \(^15\). These authors used the inward normal of each vessel wall position and respectively applied numerical differentiation and a linear least square method to obtain the spatial derivative. The availability of volumetric 3D WSS information is an improvement over existing 2D and slice-based WSS calculation methods \(^13\)\(^-\)\(^16\). These 3D methods could potentially benefit from the adaptation of smoothing splines, similar to the b-splines used by Stalder et al. for improving the robustness of the fitting procedure. \(^13\)

As was shown in simulations by Stalder et al. and later by Petersson et al., several factors hamper the calculation of WSS. Errors arise due to segmentation inaccuracies, low spatial resolution, SNR, spatial filtering and, to a lesser extent, the choice of encoding velocities (venc) \(^13\)\(^-\)\(^17\). Knowledge on these systematic errors is important for estimation of the reliability of these measurements. Simulations may help unraveling such errors. However, methods for calculating volumetric WSS at each wall position have so far not rigorously been validated by such simulations.

The goals of the current study are (1) to build on previously published algorithms \(^13\)\(^-\)\(^16\) for obtaining calculations of 3D WSS vectors and, more importantly, (2) to estimate the associated precision and accuracy in software phantoms by assessing the effects of algorithm parameters, spatial resolution and segmentation accuracy, (3) to verify these results in vivo using time-resolved PC MRI acquired in 2D slices (2D cine PC MRI) and finally (4) to show the applicability of the method by performing WSS quantification in the systolic cardiac phase of 3D cine PC MRI datasets of the carotid artery and the aorta.
3.2 Materials and methods

As detailed below, a volumetric 3D WSS method to calculate WSS was derived (3.2.1). We evaluated this method using software phantoms (3.2.2), and subsequently applied it to 2D and 3D cine PC MRI data acquired in the carotid arteries and aortas (3.2.3). All simulations and calculations were performed using in-house software developed in Matlab (version 2012b, The Mathworks, USA).

3.2.1 Wall shear stress algorithm

The input data for the algorithm consist of (i) a segmentation of the vessel lumen and (ii) the velocity vector field. Both inputs are either simulated using software phantoms or measured with time-resolved PC MRI. The output of the algorithm is a collection of WSS vectors on the vessel lumen boundary.

The segmentation of the vessel lumen boundary is represented by a surface consisting of connected triangles (3D cine PC MRI) or a polygon (2D cine PC MRI). Only velocity voxels with their midpoint inside the vessel lumen, as defined by the segmentation, are used for the volumetric 3D WSS calculations.

The edge points of these triangles and polygons are named wall points. WSS vectors ($\vec{\tau}$) were calculated on each wall point using the equation:

$$\vec{\tau} = 2\eta \dot{\epsilon} \cdot \vec{n}$$

where $\dot{\epsilon}$ the rate of deformation tensor, $\vec{n}$ the inward normal vector and the blood viscosity ($3.2 \times 10^{-3}$ Pa). Fully expanded, the WSS is given by:

$$\vec{\tau} = 2\eta \left[ \begin{array}{c} \frac{1}{2} \left( \frac{\partial v_x}{\partial x} + \frac{\partial v_x}{\partial y} \right) \frac{1}{2} \left( \frac{\partial v_y}{\partial x} + \frac{\partial v_y}{\partial z} \right) \frac{1}{2} \left( \frac{\partial v_z}{\partial x} + \frac{\partial v_z}{\partial y} \right) \frac{1}{2} \left( \frac{\partial v_y}{\partial y} + \frac{\partial v_z}{\partial z} \right) \frac{1}{2} \left( \frac{\partial v_z}{\partial y} + \frac{\partial v_z}{\partial z} \right) \end{array} \right] \cdot \vec{n}$$

To simplify this equation, two steps were performed: (i) Selection of a local coordinate system for each point on the vessel wall such that the $z'$-axis aligns with the inward normal.

$$\vec{n}(x', y', z') = \begin{bmatrix} 0 & 0 & 1 \end{bmatrix}$$

This is accomplished by rotating the original coordinate system with rotation R determined using basic vector calculus:

$$\begin{bmatrix} x' & y' & z' \end{bmatrix} = R \begin{bmatrix} x & y & z \end{bmatrix}$$

(ii) Assumption of no flow through the vessel wall, i.e. $\vec{n} \cdot \vec{v} = 0$ at the vessel wall, which is valid for large, non-porous, vessels. This reduces most terms in the equation to zero and the WSS vector in the local coordinate system is defined by:

$$\vec{\tau} = \eta \begin{bmatrix} \frac{\partial v_x'}{\partial z'} & \frac{\partial v_y'}{\partial z'} & 0 \end{bmatrix}$$

For each wall point, at least two points along the inward normal were selected onto which the surrounding velocity vectors were interpolated (18). Velocity values of zero were imposed on the
wall points (zero forcing). A smoothing spline \(^{19}\) was subsequently fitted through the velocities \((v_x'\text{ and } v_y')\) of the selected points along the inward normal. In the spline fit, the weight for the manually forced zero velocity wall point was \(10x\) lower than for the interpolated velocity points. The tolerance of the spline fit was set to \(1\%\) of the venc. The spatial derivatives \((\frac{\partial v_x'}{\partial z'}\text{ and } \frac{\partial v_y'}{\partial z'})\) on the wall were analytically derived from the fitted splines. Multiplication of the spatial velocity derivatives (shear rates) with the viscosity resulted in the WSS vectors. As a last step, the WSS vector was transformed back to the original coordinate system \([x\ y\ z]\) using the inverse rotation matrix \((R^{-1})\).

3.2.2 Software phantom simulations

Software phantoms were created to assess the effect of spatial resolution and segmentation accuracy. The software phantoms were based on a high-resolution (0.05 mm isotropic) 2D parabolic flow profile (through-plane). In this high-resolution 2D image, partial volume effects in each voxel were simulated using the average velocity for each voxel. To avoid optimal positioning of the simulated vessel with respect to the voxel, all simulations were performed 100 times with the center of the vessel shifted to different positions within the voxels. The encoding velocity (venc) was set to 10 cm/s above the maximum (center) velocity to avoid aliasing.

The homogenous theoretical WSS magnitude for cylindrical vessels with parabolic flow was calculated using \(^{20}\):

\[
WSS_{\text{theoretical}} = \eta \frac{\partial v}{\partial n} \bigg|_{n=0} = 2\eta \frac{v_{\text{max}}}{\text{radius}} 
\]  

(3.6)

Details of the performed software phantom simulations are summarized in Table 3.1; the methods for the individual simulation experiments are described below. WSS values are reported as mean WSS magnitude ± standard deviation (SD). The accuracy and precision were defined as:

\[
\text{accuracy} = 100\% \frac{\text{mean calculated WSS} - \text{theoretical WSS}}{\text{theoretical WSS}} 
\]  

(3.7)

\[
\text{precision} = 100\% \frac{\text{SD calculated WSS}}{\text{theoretical WSS}} 
\]  

(3.8)

| Table 3.1: Simulation parameters for phantom datasets. In all simulations both a calculation with and without velocity noise (10% of encoding velocity) was performed. |
|-------------|-----|-----|-----|
| Parameters                                                                                     |
|                                                               | 1   | 2   | 3   |
| Vessel diameter (mm)                                                                                     |
|                                                            6.30 | 6.30 | 6.30 |
| Center velocity (cm/s)                                                                                     |
|                                                            100 | 100 | 100 |
| Viscosity (Pa · s)                                                                                      |
|                                                            3.2 · 10^{-3} | 3.2 · 10^{-3} | 3.2 · 10^{-3} |
| Theoretical WSS (Pa)                                                                                      |
|                                                            2.13, 0.43 | 2.13, 0.43 | 2.13, 0.43 |
| Reference image resolution (mm, isotropic)                                                              |
|                                                            0.05, 0.10 | 0.05, 0.10 | 0.05, 0.10 |
| Resolution (mm, isotropic)                                                                               |
|                                                            0.5, 1.0 | 0.1 − 1.2, 0.15 − 3.0 | 0.5, 1.0 |
| Segmentation offset (mm)                                                                                 |
|                                                            0 | 0 | −1.0 − 1.0, −1.5 − 1.5 |
| Inward normal length (% diameter)                                                                          |
|                                                            5 − 100 | 50 | 50 |
| Number of points on inward normal                                                                          |
|                                                            3 − 10 | 3 | 3 |
Algorithm optimization - experiment 1

The algorithm has two customizable parameters: (i) length of the normal vector used for the spline fitting and the (ii) number of points on the inward normal. To investigate the accuracy and precision for the WSS calculations, multiple combinations of these parameters were tested (Table 3.1 experiment 1). The number of sample points on the normal was varied between 3 and 15. The length of the inward normal length was varied from 5% to 100% of the diameter. This experiment was performed both for a small 6 mm vessel (approximately the size of the common carotid artery) and a large 30 mm vessel (approximately the size of the ascending aorta). Their respective theoretical WSS values were 2.13 Pa and 0.43 Pa. The isotropic resolutions used for this experiment were respectively 0.5 mm and 1.0 mm. Additionally noise (normal distribution, the variance set to 10% of the venc [21, 22]) was added to investigate its effect on WSS estimates. The optimal parameter settings from this experiment were utilized in the remainder of this paper.

Resolution - experiment 2

In MRI, the physical resolution can be described using the point-spread function (PSF) [23]:

$$\text{PSF}(x, y) = \left( \frac{\Delta k \sin(\pi N \Delta k x)}{\sin(\pi \Delta k x)} e^{-i\pi \Delta k x} \right) \left( \frac{\Delta k \sin(\pi N \Delta k y)}{\sin(\pi \Delta k y)} e^{-i\pi \Delta k y} \right)$$

(3.9)

where $N$ is the square matrix size, $k$ the width of one k-line in k-space and $(x, y)$ the voxel coordinates. The PSF accounts for both sampling and truncation effects in k-space. Note that the PSF assumes Cartesian acquisition of k-space. We simulated the effects of variation in physical resolution by filtering a high-resolution (0.05 mm isotropic voxels) phantom using a 2D PSF, where $N$ was changed while the distance between k-lines $\Delta k$ and the other parameters were retained. This effectively resulted in a decreased k-space window with a decreased number of k-space samples. Although the physical resolution decreases after filtering with the PSF, the number of pixels remains equal. To decrease the number of pixels accordingly the PSF-filtered phantom data was down-sampled by averaging the high-resolution dataset and gridded to create pixel sizes matching the width of the PSF ($\Delta k$). Figure 3.1 visualizes the steps of this resolution reduction. The experiment was repeated after addition of noise (normally distributed, the variance set to 10% of the venc).

Segmentation - experiment 3

Effects of errors in the segmentation of the vessel wall lumen were induced by dilation and constriction of a perfect circular segmentation, while preserving the original velocity vectors in the software
phantom. Segmentation offsets between $-1$ and $1$ mm and $-2$ and $2$ mm were used to mimic segmentation errors for the $6$ mm and $30$ mm vessel, respectively.

### 3.2.3 In vivo measurements

To be able to perform PC MRI with varying spatial resolution within a reasonable scan time, we chose to verify parameter dependency of WSS in in vivo 2D cine PC MRI datasets of the left and right common carotid arteries (healthy volunteer, male, $26y$) and the ascending and descending part of the aorta in a healthy volunteer (healthy volunteer, male, $30y$). 3D cine PC MRI datasets were acquired of the carotid bifurcation (3 healthy volunteers, 1 male, $26 \pm 1y$) and the aorta (3 healthy volunteers, 2 males, $27 \pm 2y$). Approval of the local ethical committee was obtained and informed consent was provided by all 8 volunteers.

The 2D cine PC MRI aorta and carotid datasets were acquired at multiple spatial resolutions using a symmetric velocity encoding in one direction and symmetric four-point velocity encoding in three directions, respectively. The 3D cine PC MRI datasets for the carotid bifurcation and aorta were acquired with symmetric four-point velocity encoding in three directions. The $v_{enc}$ for the carotid artery was decreased in the left-right and anterior-posterior direction to increase velocity to noise ratio, see Table 3.2.

The data was acquired using a 3 T MR system (Ingenia, software version 4.1, Philips Healthcare, Best, The Netherlands) and various coils were used: the 2D cine PC MRI carotid artery measurements were performed with two surface coils positioned on both sides of the neck, the 3D cine PC MRI carotid artery measurements were performed with a dedicated eight channel carotid coil and both the 2D and 3D cine aorta measurements were done using two 16 channel phased-array coils at the posterior and anterior side of the volunteer. The carotid acquisitions were acquired with retrospective triggering with a peripheral pulse signal. The aorta acquisitions were performed with retrospective ECG triggering. The scan parameters are summarized in Table 3.2.

PC MRI datasets were corrected for systematic phase offset errors, by subtraction of phase offsets in static muscle tissue close to the vessel of interest. Aliasing artifacts were avoided by using a velocity encoding value exceeding the maximum expected velocity. Any remaining aliased voxels were corrected manually.

A 2D level set evolution algorithm (24) was used to segment the lumen for each transversal slice in the high resolution 2D cine PC MRI datasets during systole. The level set results at systole were subsequently utilized as an initial level set for the remaining cardiac phases, resulting in a time-resolved segmentation of the vessel lumen. To obtain equal temporal resolution, all lower resolution 2D cine PC MRI datasets were temporally resampled to the cardiac phases in the highest resolution dataset. Rigid spatial registration was performed to correct for patient motion in between the 2D cine PC MRI scans. The segmented vessel wall surface obtained from the highest resolution 2D cine PC MRI dataset was used in all lower-resolution datasets to avoid differences in the WSS calculation due to variations in the segmentation.

In order to check flow variations across measurements, flow was calculated by multiplication of the surface area of the segmentation and the time-averaged through-plane velocities in the segmented area. The effect of spatial resolution on calculated WSS was calculated for each cardiac phase and for the time-averaged WSS. For the 3D cine PC MRI datasets, we selected the systolic heart phase, because this cardiac phase provides the best contrast between the flowing blood and the vessel wall. The segmentations of 3D cine PC MRI data in systole (created using the active
Table 3.2: In vivo acquisition parameters of 2D cine PC MRI and 3D cine PC MRI performed in the common carotid artery and aortic arch.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Carotis 2D cine PC MRI</th>
<th>Aorta 2D cine PC MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-interpolated spatial resolution* (mm)</td>
<td>0.4 × 0.4 0.48 × 0.48 0.56 × 0.56 0.72 × 0.72 1 × 1 1.12 × 1.12</td>
<td>1 × 1 1.5 × 1.5 2 × 2 2.5 × 2.5 3 × 3</td>
</tr>
<tr>
<td>Slice thickness (mm)</td>
<td>5 5 5 5 5 5</td>
<td>5 5 5 5 5 5</td>
</tr>
<tr>
<td>Number of slices (##)</td>
<td>1 1 1 1 1 1</td>
<td>1 1 1 1 1 1</td>
</tr>
<tr>
<td>Field of view* (mm)</td>
<td>80 × 160 80 × 160 80 × 160 80 × 160 80 × 160 80 × 160</td>
<td>130 × 252 130 × 254 130 × 251 200 × 360 200 × 365</td>
</tr>
<tr>
<td>Acquisition matrix (px)</td>
<td>200 × 400 168 × 336 144 × 286 112 × 221 80 × 160 72 × 143</td>
<td>132 × 252 88 × 168 64 × 120 80 × 144 68 × 122</td>
</tr>
<tr>
<td>Flip angle (°)</td>
<td>10 10 10 10 10 10</td>
<td>20 20 20 20 20 20</td>
</tr>
<tr>
<td>TE (ms)</td>
<td>9.3 8.1 7.2 6.0 4.8 4.5</td>
<td>3.5 2.7 2.4 2.3 2.3</td>
</tr>
<tr>
<td>TR (ms)</td>
<td>20 20 20 20 20 20</td>
<td>5.6 4.2 3.9 3.6 3.5</td>
</tr>
<tr>
<td>Velocity encoding directions* (##)</td>
<td>3 3 3 3 3 3</td>
<td>1 (FH) 1 (FH) 1 (FH) 1 (FH) 1 (FH)</td>
</tr>
<tr>
<td>Velocity encoding values* (cm/s)</td>
<td>60 × 60 × 100 60 × 60 × 100</td>
<td>200 200 200 200 200</td>
</tr>
<tr>
<td>Acceleration</td>
<td>n.a. n.a. n.a. n.a. n.a. n.a.</td>
<td>SENSE 2 SENSE 2 SENSE 2 SENSE 2 SENSE 2</td>
</tr>
<tr>
<td>Heart phases</td>
<td>15 15 15 20 20 20</td>
<td>30 30 30 30 30 30</td>
</tr>
<tr>
<td>Non-interpolated temporal resolution (ms)</td>
<td>87 81 83 83 84 81</td>
<td>33 30 32 30 29</td>
</tr>
<tr>
<td>Average heart rate during scan (bpm)</td>
<td>55 59 58 58 57 59</td>
<td>61 66 62 66 66 68</td>
</tr>
<tr>
<td>Scan duration (s)</td>
<td>412 338 288 221 162 145</td>
<td>130 88 72 77 65 65</td>
</tr>
</tbody>
</table>

* AP × RL ( × FH); SENSE: sensitivity encoding reduction factor; TFE: transient field echo turbo factor
Table 3.2: (continued) In vivo acquisition parameters of 2D cine PC MRI and 3D cine PC MRI performed in the common carotid artery and aortic arch..

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Aorta 3D cine PC MRI</th>
<th>Carotis 3D cine PC MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-interpolated spatial resolution* (mm)</td>
<td>$2 \times 2 \times 2$</td>
<td>$0.63 \times 0.63 \times 0.65$</td>
</tr>
<tr>
<td>Field of view* (mm)</td>
<td>$217 \times 80 \times 217$</td>
<td>$135 \times 135 \times 30$</td>
</tr>
<tr>
<td>Acquisition matrix (px)</td>
<td>$108 \times 40 \times 108$</td>
<td>$216 \times 216 \times 46$</td>
</tr>
<tr>
<td>Flip angle ($^\circ$)</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td>TE (ms)</td>
<td>3.5</td>
<td>3.1</td>
</tr>
<tr>
<td>TR (ms)</td>
<td>8</td>
<td>6.7</td>
</tr>
<tr>
<td>Velocity encoding directions* (#)</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Velocity encoding values* (cm/s)</td>
<td>$183 \times 183 \times 183$ ($\pm 29$)</td>
<td>$60 \times 60 \times 100$</td>
</tr>
<tr>
<td>Acceleration</td>
<td>SENSE 2, TFE 2</td>
<td>SENSE 2, TFE 8</td>
</tr>
<tr>
<td>Heart phases</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>Non-interpolated temporal resolution (ms)</td>
<td>$81.5 \pm 1.6$</td>
<td>$145.7 \pm 22.3$</td>
</tr>
<tr>
<td>Average heart rate during scan (bpm)</td>
<td>$61.3 \pm 1.2$</td>
<td>$60 \pm 8.4$</td>
</tr>
<tr>
<td>Scan duration (s)</td>
<td>$1536 \pm 68$</td>
<td>$434 \pm 24$</td>
</tr>
</tbody>
</table>

* AP × RL (× FH); SENSE: sensitivity encoding reduction factor; TFE: transient field echo turbo factor

contour evolution algorithm in ITK-SNAP (25) were filtered with a Laplacian filter (26) to reduce irregularities and discretization effects and the results were manually checked by overlaying them on all image types (velocity, magnitude images). The WSS was calculated and visualized using arrows and colored surfaces. Each arrow corresponds to a calculated WSS vector at that specific wall position on the vessel wall surface.

3.3 Results

Algorithm optimization - experiment 1

Figure 3.2 shows the results of variation of the algorithm parameters (Table 3.1, experiment 1). The effects on accuracy and precision are similar for both vessel sizes. Both the accuracy and precision improve when choosing fewer points on the inward normal or a large inward normal length, i.e. a long distance between fitted velocities. This was also the case when noise was added, although the precision decreased compared to the simulation without noise. Based on these data we decided to use an inward normal length of at least 50% of the diameter and 3 points, including the wall point ($v_{wall} = 0$ cm/s), on the inward normal to use as input for the smoothing spline fitting algorithm. These parameters correspond to the areas marked by the red boxes in Figure 3.2.

Resolution - experiment 2

Figure 3.3a and Figure 3.3b show the effects of varying resolution on the calculated WSS. Simulations at all resolutions on average underestimated the true WSS. However, both under- and overestimations were found on the individual wall points, likely depending on the distance between the vessel wall and the closest voxel. Overall, estimated WSS further decreased at lower resolution, resulting in increasingly impaired accuracy. Additionally, the precision of WSS calculation decreased with increasing voxel size. The precision for datasets with added noise was lower, but this effect was less pronounced for larger voxel sizes. At voxel sizes used in conventional protocols, the accuracy was 4.3 to 4.6% and the precision 19 to 22%, assuming an isotropic resolution of 0.7 mm for the carotid and 2.0 mm for the aorta protocol.
Figure 3.2: Effect of inward normal vector length and number of points along the normal vector on the WSS calculation (experiment 1) on precision and accuracy for a 6 mm vessel and b for a 30 mm vessel with and without added noise. Noise is normally distributed, with the variance set to 11 cm/s (10% of the venc). The red rectangle shows the most optimal range of settings.

Segmentation - experiment 3

Figure 3.3 c and Figure 3.3 d show the effects of segmentation offsets on the calculated WSS in the phantom vessels. For wider segmentation (positive offset), the calculated WSS decreased, while the precision of the WSS calculation remained equal. For narrower segmentation, the calculated WSS increased rapidly. The algorithm performed similarly after addition of noise to the data. Assuming half the voxel size (respectively 0.25 and 1.0 mm) as segmentation accuracy, the accuracy of calculated WSS can be as low as 30% and 40% for the 6 mm and 30 mm vessels, respectively.

In vivo measurements - 2D cine PC MRI

The average flow rates for each resolution were found to deviate by less than 10% from the value obtained at 0.4 mm resolution. The level set segmentation in the left and right carotid artery for both the systolic (defined as highest flow rate) and diastolic (defined as lowest flow rate) time points are shown in Figure 3.4 a and Figure 3.4 b (diastole) and Figure 3.4 c and Figure 3.4 d (systole).
Volumetric arterial wall shear stress calculation based on cine phase contrast MRI

Figure 3.3: Results from the WSS calculations in multiple software phantoms. The theoretical WSS (blue line), the simulated WSS without noise (green line), and the simulated WSS with noise (red line) with the accompanying standard deviations (dashed lines) are displayed. Noise is normally distributed, with the variance set to 11 cm/s (10% of the venc). a,b: Resolution variation versus calculated WSS. c,d: Segmentation offsets versus simulated mean WSS at software phantom resolutions of 0.5 mm and 1 mm, respectively. Negative offsets represent a constricted (smaller) segmentation; positive offsets represent a dilated (larger) segmentation.

The results for the WSS calculations are shown in Figure 3.4 e and Figure 3.4 f. Overall the WSS magnitude increased in systole. Higher resolutions generally lead to a higher average WSS with a few exceptions. Investigation of these exceptions revealed a lower flow in those measurements (e.g. Figure 3.4 e, 0.4 mm resolution, at 582 ms). The spatially averaged WSS values in the common carotid artery ranged from 0.2 (diastole) to 6 Pa (systole). The spatiotemporal average WSS was 0.95 ± 0.78 Pa.

Figure 3.5 shows similar data for the ascending and descending aorta. The absolute flow rates for each resolution were found to deviate by approximately 5% from the value obtained at 1 mm resolution. Figure 3.5 a-d show the level set segmentations of the ascending and descending aorta, for both diastole (Figure 3.5 a,c) and systole (Figure 3.5 b,d). As can be seen in Figure 3.5 a-d, the level set segmentation is based on intensity on the magnitude image with the highest resolution and is less accurate in diastole than systole. Despite some minimal automatic segmentation errors, the resulting resolution-dependent average WSS estimates, as shown in Figure 3.5 e and Figure 3.5 f, show a lower average WSS magnitude for lower resolution datasets. The average WSS magnitude in the ascending aorta was 0.05 to 6.9 Pa with a time-averaged WSS of 0.57 ± 0.70 Pa. In the
Figure 3.4: 2D cine PC MRI data in the left (left column) and right (right column) carotid artery of a healthy volunteer. a, b The first (diastole) and c, d second (systole) rows show the wall delineation for magnitude and velocity images at all acquired spatial resolutions. e, f The last row shows the calculated WSS values for the acquired spatial resolutions at each cardiac phase; the last graph in also shows the standard deviation due to physiological spatiotemporal WSS variation.

descending aorta the average WSS magnitude ranged from 0.09 to 11.9 Pa with a time-averaged WSS of $0.9 \pm 1.10$ Pa.

In vivo measurements - 3D cine PC MRI

Figure 3.6 a and Figure 3.6 b show the calculated WSS vectors at peak systole in the carotid bifurcation and aorta, respectively. The average WSS in the carotid bifurcations in systole was $1.34 \pm 0.72$ Pa, with values ranging from 0.03 to 4.82 Pa. The average WSS in the aortas in systole was $1.07 \pm 0.42$ Pa, with values ranging from 0 to 4.48 Pa. In both measurements we found a complex pattern of WSS, with substantial spatial gradients in both WSS magnitude and direction.

3.4 Discussion

We have presented and evaluated an approach to determine volumetric WSS in arteries. The volumetric WSS calculation method put forward here differs from existing methods in several aspects. Rather than presenting WSS in a manually placed slice perpendicular to the vessel wall.
Volumetric arterial wall shear stress calculation based on cine phase contrast MRI

or a segment of the vessel wall (15), we quantify WSS at all points on the entire vessel wall. Thus, it is possible to detect abnormal regional variations that a slice or segmental based method would miss. This increase of spatial WSS resolution comes at the expense of the number of velocity measurements that is used for each fit at the wall. To minimize errors, we applied natural neighbor interpolation combined with a smoothing spline fit at each vessel wall point. Natural neighbor interpolation provides a continuous first derivative in contrast to methods using Lagrangian interpolation (27). As indicated by the accuracy results in this study, the smoothing spline provides better fits in the presence of noisy velocity data than linear or parabolic methods (17). Other methods combine the interpolation and fitting step by fifth-order polynomial fitting of the 3D cine PC MRI velocities (28, 29), but up to now, this approach has only been applied in phantom datasets. We showed that the accuracy of WSS is optimal when an inward normal length of 50% vessel diameter is used with 3 equidistant velocity points. This is relatively long compared to literature (6, 12, 14, 15, 30), which may be related to the parabolic velocity profiles that were used in our simulations. The use of only three points on the inward normal may smooth complex in vivo velocity profiles (31), resulting in WSS underestimations. More research is needed to further optimize the algorithm parameters in areas of complex velocity patterns.

Figure 3.5: 2D cine PC MRI data in the ascending (left column) and descending (right column) aorta of a healthy volunteer. a,b The first (diastole) and c,d second (systole) rows show the wall delineation for magnitude and velocity images at all acquired spatial resolutions. e,f The last row shows the calculated WSS values for the acquired spatial resolutions at each cardiac phase; the last graph in also shows the standard deviation due to natural spatiotemporal WSS variation on the vessel wall.
Figure 3.6: Visualization of the WSS vectors as calculated directly from the 3D cine PC MRI datasets of six volunteers in a the carotid bifurcation and b the aorta in the systolic heart phase.

The effects of spatial resolution have been described previously (13, 27), but may differ significantly between fitting methods (17). A higher spatial resolution improves WSS calculations, but practical limitations exist, related to field strength and scan duration. Based on our software phantom experiments we conclude that spatial resolution of PC MRI data for WSS calculation should be such that at least 8 voxels are available across the diameter in order to obtain 5% accuracy. A guideline on resolution of flow quantification using PC MRI suggested at least 3 voxels across the diameter (32), and 16 isotropic voxels over the vessel lumen area (4.5 voxels across the diameter) (33). This difference results from WSS being related to the derivative of the velocity field as opposed to flow as an integration of this field. Our simulations show that the average
Volumetric arterial wall shear stress calculation based on cine phase contrast MRI

WSS is generally underestimated. The predictions are in contrast to analyses of Petersson et al., who found an overestimation of WSS at similar resolution and similar WSS magnitude (17). Other authors (13, 27) found an even larger underestimation at similar resolution. These differences are likely related to the used fitting methods (parabolic, linear vs. spline fitting).

The spatial resolution was also found to be critical for calculation of WSS in the in vivo 2D cine PC MRI data. Although we did not have a gold standard for the WSS magnitude in vivo, the 2D cine PC MRI data showed that the spatially averaged WSS converged towards higher values at higher spatial resolutions, similar to what was found for the phantom data. However, the spatial resolution effect in the in vivo 2D cine PC MRI data was larger than in the phantom data, suggesting the presence of steeper velocity gradients in vivo that are more prone to be underestimated.

The larger spatial variation of in vivo WSS at higher resolutions compared to the software phantoms may partly be due to noise, related to the MRI signal, and movement artifacts. However, there is also a contribution from the asymmetry of the flow profiles. WSS calculations based on low-resolution datasets may not be able to capture the variations occurring at a smaller spatial scale, and are thus biased towards a spatial average. Resolutions as high as 0.4 mm in the carotids seem therefore be mandatory when studying local changes in WSS, whereas lower resolutions may suffice if systemic disease and general patterns of WSS are studied.

Despite similar resolution-dependency of WSS estimates in 2D cine PC MRI datasets of carotid arteries and the aorta, we noticed that the aorta data were more consistent to the phantom experiments than those on the carotids. This can be attributed to a better velocity-to-noise ratio and a higher temporal resolution in the aorta scan, both of which improves the quality of the segmentations and the velocity measurements.

Our data show that segmentation is an important factor for determining the accuracy and precision of WSS calculations. Although the effect of segmentation errors is large, little quantitative information is available in literature. Studies have proposed to improve the segmentation by making use of the velocity profile (16). One recent study described the effect on WSS magnitude by changing the voxel location with respect to the wall (17). Given the large influence of segmentation errors, we advise (i) to always use a time-resolved segmentation to account for wall motion and (ii) to thoroughly check the segmentations for every slice and every heart phase on any of the available images (magnitude and velocity images).

Compared to other literature, our in vivo WSS values in the aorta are rather high. Publications using the method by Stalder et al. are consistent in reporting values up to 1.1 Pa (8, 13, 34). Other PC MRI-based methods report even lower values (15, 35), while CFD-based WSS calculations report higher WSS values in the aorta (36). The larger WSS values compared with other PC MRI-based techniques may be due to the fact that the current volumetric approach does not use any spatial filtering before calculating the WSS values and is therefore less prone to spatial blurring that lowers the average WSS.

In the carotid artery, the WSS calculations in literature are mainly based on ultrasound velocity measurements (0.5 – 1.0 Pa, (37, 38)) and 2D cine PC MRI (0 – 2.5 Pa, (6, 39, 40)). For the carotid artery, our WSS calculations at the highest resolution of 0.4 mm match the WSS magnitude values reported in recent literature.

A limitation of the phantom study was the use of only parabolic velocity profiles in the simulations. Further research is needed to investigate the effect of complex flow on WSS calculation. A limitation of the in vivo 2D cine PC MRI measurements was that in the aorta the measurements were performed with unidirectional velocity encoding, whereas in the carotids the velocity measure-
ments were performed in three directions. The 3D cine PC MRI study acquisition of the carotid bifurcation was limited by a low temporal resolution, which has likely caused underestimation of the average and peak WSS. Another limitation can be the use of parallel imaging (SENSE), which may decrease the SNR (41). Because we used a relatively low acceleration factor, the effect of SENSE on the velocity measurements is expected to be limited (42).

In the future the method presented here may provide a WSS reference map of a vessel, which could be used in the (early) identification of pathologies. The next step towards clinical applicability will be to further validate the described method on complex geometries, where the estimates can be compared with CFD simulations, which are generally considered as the gold standard (14, 43, 44).

### 3.5 Conclusion

In conclusion, volumetric WSS calculation provides spatiotemporal information on WSS magnitude. Even with optimized algorithm parameters, the results of WSS calculations are strongly dependent on segmentation and resolution. To obtain reliable WSS estimates, we advise to first acquire of a high-resolution 3D cine PC MRI, including at least 8 voxels across the diameter of the targeted vessel, which is subsequently segmented using a time-dependent, manually checked method. Smoothing splines of velocity profiles over 50% of the diameter and including 3 points along the inward normal should be applied to calculate the WSS.

### Bibliography


44. van Ooij P, Guedon A, Poelma C, Schneiders J, Rutten MCM, Marquering HA, Majoie CB, vanBavel E, and Nederveen AJ. Complex flow patterns in a real-size intracranial aneurysm phantom: phase contrast