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Potters, W.V.

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

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The effect of temporal and spatial resolution of cine phase contrast MRI on wall shear stress and oscillatory shear index assessment

Merih Cibis*
Wouter V. Potters*
Frank J.H. Gijsen
Henk A. Marquering
Pim van Ooij
Ed van Bavel
Jolanda J. Wentzel
Aart J. Nederveen

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SUBMITTED (2015)

* shared first authorship
6.1 Introduction

Atherosclerotic plaques develop at the sites of low wall shear stress (WSS) in the arteries (1,2). Besides WSS magnitude, some studies show that oscillatory changes of the WSS direction may promote atherogenesis (3-5). Such oscillations within the cardiac cycle are quantified by the Oscillatory Shear Index (OSI) (6,7). Although both WSS and OSI contribute to initiation and progression of atherosclerotic disease, most studies focus only on the WSS magnitude and exclude analysis of OSI due to the challenge of obtaining accurate WSS magnitude and OSI simultaneously (8-12).

WSS magnitude is calculated by multiplying blood viscosity with wall shear rate (WSR), the latter being the first radial derivative of blood velocity at the vessel wall. The velocity field in the artery that is necessary to calculate WSR is generally obtained with computational fluid dynamics (CFD). CFD is a powerful simulation tool that enables prediction of blood velocities and related hemodynamic parameters (13,14). However, CFD requires accurate boundary conditions, non-clinical expertise and extensive computational resources and time. Alternatively, the velocities can be obtained by phase contrast MRI (PC MRI) measurements (15-18). However, the WSS values based on MRI depend on the spatial resolution of PC MRI (19-23). In a recent study, we showed that WSS estimates based on in vivo PC MRI data have a realistic representation of the spatial distribution but underestimate magnitude, due to the limited spatial resolution of PC MRI (19). Stalder et al. also investigated the effect of spatial resolution on flow and WSS using synthetic data (17) and showed that the WSS values calculated with the method they proposed were strongly affected by the spatial resolution. Petersson et al. showed that higher true WSS values were underestimated more by PC MRI and reducing the resolution enhanced the underestimation (20). These findings suggest that the spatial resolution of PC MRI measurements should be sufficiently high to obtain the magnitude of WSS accurately. OSI, on the other hand, is a measure of temporal changes of WSS. An accurate estimation of OSI might, therefore, only be possible with both sufficiently high spatial and temporal resolutions of PC MRI measurements.

The MRI settings such as the spatiotemporal resolution involve a trade-off between the measurement duration and the accuracy of the flow, WSS and the OSI estimations. To perform the measurement within clinically feasible scan time, the resolution is generally kept low and the accuracy of these parameters is given away. One can, however, argue that each estimated parameter is affected differently. To our knowledge, none of the previous studies has investigated the effect of spatial and temporal resolution together on these hemodynamic parameters extensively. Our objective was to evaluate the effect of resolution on the assessments of flow, WSS and OSI that we obtained from 2D cine PC MRI scans of a carotid artery phantom at different spatial and temporal resolutions.

6.2 Methods

6.2.1 Phantom and flow set-up

A silicone phantom was built based on the surface reconstruction of a healthy right carotid artery (age 25 years) acquired from a previous study (19) (Figure 6.1 a). The phantom was connected to a flow set-up (Figure 6.1 b). The set-up consisted of a computer, computer controlled pulse generator, an air pressure controller (LifeTec Group, Eindhoven, The Netherlands) and a closed flow
phantom circuit filled with water. The computer, the pulse generator, the air pressure controller, and the flow meter were placed outside the MRI room. The phantom circuit, including an MR compatible pump system, was placed on the MR table connected to the phantom. The pump system consisted of thin-walled silicone cylinders that were filled with water and embedded in a rigid air-filled enclosure. Air pressure in the rigid enclosure was varied to dilate and contract the water-filled cylinders. One-way valves ensured that this cyclic air pressure induced a pulsatile flow. The shape and the magnitude of the flow waveform were set by adjusting the shape and the amplitude of the cyclic air pressure wave. The shape of the waveform was then tuned by adjustment of resistors and capacitors within the closed fluid circuit. A real-time ultrasound flow probe was used to calibrate the PC MRI measured flow waveform before the MRI scans outside the MRI room while keeping all experimental conditions the same.

### 6.2.2 MRI acquisition

The carotid phantom was scanned with a 3 T MR system (Ingenia, software version 4.1.3, Philips Healthcare, The Netherlands) using a solenoid rat coil. 2D cine PC MRI scans were performed at two planes with velocity encoding in 3 directions using various temporal and spatial resolutions as shown in **Figure 6.4** in red circles (venc: 100 cm/s, TR: 8.9 – 24.1 ms, TE: 4.67 – 6.57 ms, flip angle: 10°). We performed thirty measurements at different spatial and temporal resolutions at two planes, which took between 1.1 and 21.0 minutes per measurement depending on the spatiotemporal resolution.
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Figure 6.2: a Flow waveforms at different spatial (sr) and temporal (tr) resolutions. Black lines show the PC MRI measurements and the red line shows the ultrasound probe measurement. Spatial resolution varied between 0.2 mm and 1 mm and the temporal resolution varied between 9.1 ms and 142.9 ms. b Ultrasound probe vs. PC MRI flow measurements.

resolution. All measurements were performed on the same day without an interruption of the flow setup to prevent any changes in the pulse shape. The flow stability was verified with the ultrasound flow probe before and after the MR session. While the typical velocity profile in the common carotid artery (CCA) is closer to a parabolic shape, it is more skewed in the internal carotid artery (ICA) as shown in Figure 6.1 c. Hence, the WSS and OSI distributions are different between CCA and ICA. To analyze both velocity profiles and to avoid MR table movement in between positions, we chose the first plane 1 cm proximal to the branching point perpendicular to CCA and the second plane 1 cm distal to the branching point perpendicular to ICA. All the acquisitions were performed with retrospective triggering, except those requiring a temporal resolution below 30 ms. For acquisitions with temporal resolution below 30 ms, prospective triggering was used to be able to measure separate flow encoding directions in separate heart cycles. All PC MRI data was corrected for first-order phase offset errors.

6.2.3 Segmentation

The vessels were automatically segmented on the MRI measurement planes by an in-house tool written in MATLAB. Initial segmentation was performed by k-means clustering, followed by an active contour segmentation using the method by Herment et al. A separate segmentation was performed for each measurement. The segmentation performed on the images at the highest spatial resolution (0.2 mm) will be denoted as the ‘best segmentation’ in the rest of this article.

6.2.4 WSS calculations based on PC MRI

Since the workflow for WSS calculations based on PC MRI was discussed before in detail, we give a short overview only. Firstly, the inward normal was determined for each point on the surface. The velocities measured by PC MRI were interpolated along the inward normal direction at 2 points at a distance of 1.5 and 3 mm from the wall. The velocity at the surface was set to zero, and a spline curve was fitted through these two velocity vectors with inclusion of the zero velocity point at the wall. By taking the gradient of the curve at the point on the wall, wall shear rate (WSR)
was calculated. WSS was calculated by multiplying WSR with the dynamic viscosity of water which
was assumed to be $1.0 \cdot 10^{-3}$ Pa · s. rop

### 6.2.5 OSI Calculations

The commonly used definition of OSI was introduced by He and Ku (7) as follows:

$$\text{OSI}(\vec{s}) = 0.5 \left( 1 - \frac{\sum_{t=0}^{T} |\vec{WSS}(\vec{s}, t)| \delta t}{\sum_{t=0}^{T} |\vec{WSS}(\vec{s}, t)| \delta t} \right)$$  \hspace{1cm} (6.1)

where $\vec{s}$ is the position at the vessel wall, $t$ is the time point, $\delta t$ is time step, and $T$ is the number of
time steps within the cardiac cycle. The OSI varies between 0 and 0.5 where higher OSI indicates
larger changes in the WSS direction.

### 6.2.6 Analysis

The flow waveforms measured in the CCA were compared with the ultrasound flow probe measure-
ments. For different spatiotemporal resolutions, we analyzed cross-sectional area, mean flow, peak
flow, WSS, and OSI at the CCA and ICA. The WSS values were firstly averaged over the cardiac
cycle and subsequently over the circumference of the vessel wall. The OSI values were averaged
over the circumference of the vessel wall. Furthermore, to study the local distribution of WSS and
OSI over the circumference, WSS and OSI values were averaged separately over the quarters of the
vessels. Finally, to investigate the effect of segmentation on the estimated hemodynamic param-
eters, the 'best segmentation' was applied to each dataset. The mean flow, WSS and OSI were
obtained with the best segmentation and compared with those obtained with the segmentation per
measurement.

### 6.2.7 Statistical analysis

The associations between spatiotemporal resolutions and the hemodynamic parameters and between
the results based on the measurement-specific segmentations and best segmentation were tested by
linear regression analysis. In statistical evaluations, the level of significance was chosen at $P < 0.05$.
The results were represented as the mean ± standard deviation of the 30 measurements.

### 6.3 Results

The linear regression coefficients and the slopes of the linear regression lines (in %/mm and
%/100ms) between the hemodynamic parameters and spatiotemporal resolution are summarized
in Table 6.1.

### 6.3.1 Flow waveform at CCA

Flow waveforms obtained from PC MRI measurements at the highest and the lowest spatial and
temporal resolutions are shown in Figure 6.2 a. The red line shows the flow waveform based on
the ultrasound probe measurement. At the highest spatial resolution (0.2 mm) and the highest
temporal resolution (24.4 ms, black dashed line), the shape of the flow waveform was similar to the one measured by the ultrasound probe. At the lowest spatial resolution (1.0 mm) and the highest temporal resolution (9.1 ms, light blue dashed line), the shape of the flow waveform was still captured although peak flow was underestimated (7.8 mL/s). At lowest temporal resolution (142.9 ms, red and orange dashed lines), the peak flow was shifted backward in the cardiac cycle and was underestimated. The ultrasound probe measurements were plotted against the PC MRI measured flows in Figure 6.2b which shows underestimation of flow at higher flows in all cases except for the measurement at the highest spatial and temporal resolution.

### 6.3.2 Area, mean flow, and peak flow at CCA and ICA

The cross-sectional area was 24.6 ± 0.6 mm² at the CCA and 29.0 ± 2.9 mm² at the ICA. The mean flow based on PC MRI measurements was 2.5 ± 0.2 mL/s at the CCA and 1.3 ± 0.2 mL/s at the ICA (Figure 6.4). The mean flow is plotted for the different spatial resolutions in Figure 6.3a and for the different temporal resolutions in Figure 6.3b. A significant association was found between mean flow and the spatial resolution (slope − 13.0 %/mm for the CCA and − 49.0 %/mm for the ICA). No correlation was observed between mean flow and temporal resolution. The mean flow based on the ultrasound flow probe measurement was 2.7 ± 0.02 mL/s at CCA; hence, the ratio of the mean flows based on PC MRI measurements and the ultrasound flow probe measurement was 95.1 ± 7.9%.

The peak flow was 7.6 ± 1.0 mL/s at CCA and 4.2 ± 0.6 mL/s at ICA (Figure 6.4). The peak flows at different spatiotemporal resolutions are shown in Figure 6.3c and Figure 6.3d. At the highest spatial resolution (0.2 mm) and the highest temporal resolution (24.4 ms), the peak flow was estimated accurately (9.1 mL/s) relative to ultrasound probe peak flow measurement (9.1 mL/s). At lower spatiotemporal resolutions, peak flow was underestimated. The estimated peak flow was significantly dependent on both spatial (− 17.0 %/100ms for ICA) and temporal resolution (− 19.0 %/100ms for CCA to − 24.0 %/100ms for ICA).
Figure 6.3: a Mean flow [mL/s] vs spatial resolution [mm] b Mean flow [mL/s] vs temporal resolution [ms] c Peak flow [mL/s] vs spatial resolution and d Peak flow [mL/s] vs temporal resolution at CCA and at ICA. Red lines show the mean and peak flow measured by ultrasound echo probe.

6.3.3 Mean WSS at CCA and ICA

The WSS at different spatial and temporal resolutions are shown for CCA and ICA in Figure 6.6 a and Figure 6.6 b. The WSS was 0.12 ± 0.01 Pa at the CCA and 0.09 ± 0.02 Pa at the ICA (Figure 6.5). At the highest spatial resolution (0.2 mm) and the highest temporal resolution (24.4 ms), WSS was determined as 0.15 Pa at the CCA and 0.14 Pa at the ICA. At lower spatial resolutions, the estimated WSS was lower. We found a significant inverse relationship between the estimated WSS and the spatial resolution (−19.0 %/mm for the CCA and −33.0 %/mm for the ICA). No relationship was found between mean WSS and temporal resolution.

6.3.4 OSI at CCA and ICA

Figure 5.6 c and Figure 5.6 d show OSI at different spatial and temporal resolutions for the CCA and ICA. OSI was found 0.02 ± 0.02 at the CCA and 0.08 ± 0.05 at the ICA (Figure 5.5). The highest OSI values were found at the highest spatial resolution (0.2 mm) and the highest temporal resolution (24.4 ms), which were 0.08 for the CCA and 0.27 for the ICA. The OSI was underestimated at lower spatiotemporal resolutions. We found a significant association between OSI and spatial resolution in the CCA (−26.0 %/mm), but the association between OSI and temporal resolution was not significant in the CCA. In the ICA, we only found a significant association between OSI and temporal resolution (−16.0 %/100ms).
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Figure 6.4: Mean flow of a CCA and b ICA at different spatial and temporal resolutions. Red circles show the measurement points. Peak flow of c CCA and d ICA at different spatial and temporal resolutions. Red circles show the measurement points. White lines show the measurement durations of 18, 6 and 2 minutes (left to right).

6.3.5 Local WSS distribution

The mean WSS of each quarter for four measurements in the CCA and the ICA is shown in Figure 6.7. For the CCA, the highest WSS quarter was the bottom right quarter (0.14 ± 0.01 Pa) and the lowest WSS quarter was the top left quarter (0.07 ± 0.02 Pa). These highest and the lowest of WSS regions were found in all measurements for the CCA regardless of spatial and temporal resolution. For the ICA, the highest WSS quarter was the bottom right quarter (0.13 ± 0.02 Pa) which was found in all measurements. The lowest WSS quarter for the ICA was the top left quarter (0.04 ± 0.02 Pa) which was found in 28/30 measurements (93%).

6.3.6 Local OSI distribution

The mean OSI of each quarter for four measurements is shown in Figure 6.8. OSI was generally low in all quarters of the CCA. The highest OSI quarter in the CCA was the top left quarter (0.04 ± 0.02) which was found in 23/30 measurements (77%). The lowest OSI quarter was bottom right quarter, (0 ± 0.01) and found in 29/30 (97%) measurements. For ICA, the highest OSI quarter was top left quarter (0.20 ± 0.08) and the lowest OSI quarter was the bottom right quarter (0.01 ± 0.01) which was found in all measurements regardless of spatial and temporal resolution.
Figure 6.5: WSS of a CCA and b ICA at different spatial and temporal resolutions. Red circles show the measurement points. OSI of c CCA and d ICA at different spatial and temporal resolutions. Red circles show the measurement points. White lines show the measurement durations of 18, 6 and 2 minutes (left to right).

6.3.7 Calculations using fixed segmentation at CCA

The best segmentation resulted in the cross-sectional area of 24.7 mm² for the CCA. The results based on the best segmentation were very similar to those based on the segmentations per measurement. The flow obtained with the best segmentation was 2.7 ± 0.2 mL/s which was in agreement with the ultrasound probe flow measurements and 8.0% higher than that obtained with the measurement specific segmentations (2.5 ± 0.2 mL/s, r² = 0.85, P < 0.001). We found no significant correlation between the mean flow and spatial resolution after switching to the best segmentation (r = -0.09, P = 0.62). The WSS with the best segmentation showed good agreement with that based on the measurement specific segmentations (r² = 0.99), which were on average only 2% lower in magnitude (0.11 ± 0.01 Pa, P < 0.001). The mean OSI based on the best segmentation was 0.02 ± 0.02 which was also in good agreement with that based on the measurement specific segmentations (r² = 0.99).

6.4 Discussion

In this study, we investigated the influence of spatial and temporal resolution on the estimation of mean flow, peak flow, WSS and OSI in a realistic phantom of a carotid bifurcation. Our results show that not all parameters are affected to the same extent by spatial and temporal resolution. For example, mean flow was not dependent on the temporal resolution; but it was influenced by
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Figure 6.6: a) WSS [Pa] vs spatial resolution [mm], b) WSS [Pa] vs temporal resolution [ms], c) OSI vs spatial resolution and d) OSI vs temporal resolution at CCA and at ICA.

Figure 6.7: The mean WSS [Pa] of each quarter at different spatial and temporal resolutions in CCA and in ICA. * shows the highest WSS quarter and + shows the lowest WSS quarter.
Figure 6.8: The mean OSI of each quarter at 4 different spatial and temporal resolutions in CCA and in ICA. * shows the highest OSI quarter and + shows the lowest OSI quarter.

The estimated flow waveform and the peak flow were mainly dependent on temporal resolution. To obtain the peak systolic time point within the cardiac cycle and the peak systolic flow accurately, it was necessary to perform the acquisition at a high temporal resolution. The higher temporal resolution also reduced flattening of the flow waveform. At a temporal resolution lower than 50 ms, the error in the estimated peak flow was still more than 10%.

The WSS values were specifically relying on high spatial resolution. The observed effects of spatial resolution on average WSS magnitude are in correspondence with existing literature. The typical underestimation of WSS, when quantified by PC MRI, has been described extensively \cite{17,20,22,26,27}. For a parabolic flow with a flow rate equal to the measured CCA mean flow, the theoretical WSS value is approximately 0.15 Pa. Since the velocity profile at CCA was close to a parabolic shape, the WSS was expected to have a value close to the theoretical WSS value. Only at a spatial resolution of 0.2 mm, the WSS based on PC MRI was close to the theoretical value and underestimated at lower resolutions. However, the changes in the spatial resolution at lower spatial resolutions had only a marginal impact in the estimated WSS value, e.g. a decrease of 0.1 mm in spatial resolution only decreases the WSS by 2 – 3%. Note that the duration of our 2D PC MRI measurements at spatial resolution of 0.2 mm and temporal resolution of 24 ms was 21 minutes at only one plane which is not feasible in the clinic. Furthermore, the noise level increases with the increase of spatial resolution, even more if a standard receive coil is used. Nevertheless, recent developments in MRI acceleration technologies will lead to shorter scan times and/or decreased
noise levels at high resolutions (28, 29), which, in time, will allow faster and more accurate WSS based on PC MRI.

The effects of temporal resolution on time-resolved WSS parameters have not been investigated previously. We found that the WSS values averaged over the cardiac cycle were not dependent on the temporal resolution. For the CCA, OSI was dependent on spatial resolution, but not on temporal resolution. For the ICA, OSI was dependent on temporal resolution, but not on spatial resolution. This is likely due to the low OSI in the CCA and the high OSI in the ICA. OSI values were higher at high spatial and temporal resolutions. However, at lower spatiotemporal resolutions, the changes in the spatiotemporal resolutions affect the estimated OSI values only to a limited extent.

Despite underestimation of the WSS and the OSI magnitude, the locations of low and high WSS and OSI regions showed a good agreement in most of the measurements, regardless of spatiotemporal resolution. This result together with the limited dependency of WSS and OSI values on the chosen spatiotemporal resolutions indicates that WSS and OSI can be compared between studies with similar PC MRI protocols.

Although the segmentation had an influence on the estimated flow, the effect of segmentation on WSS and OSI was found to be small. This may be related to the fact that choosing zero velocity at the wall improves the robustness of WSS estimations, as shown by Petersson et al. (20).

In this study, we used a carotid flow profile of the CCA and the ICA, which represents two typical velocity profiles inside carotid arteries. We therefore expect that our results on the effect of spatiotemporal resolutions are representative for other areas of the carotid arteries and other vessels with similar velocity profiles.

This study had three main limitations. Firstly, we limited the study to only 2D PC MRI measurements (with 3D velocity encoding) within the carotid artery. We chose to perform 2D acquisition to keep the MRI scans within clinically acceptable scan times since high-resolution 4D PC MRI measurements would result in unacceptable long scan times. To overcome this limitation, we chose two MRI measurement planes, one at CCA, and one at ICA, representing the relevant two velocity profiles. Secondly, we performed only in vitro measurements, which do not necessarily represent in vivo situation. However, the long scan times would again be the limitation to perform measurements at very high spatial and temporal resolutions. Finally, we used water as the medium instead of a blood representing fluid. However, the effect of blood viscosity on the estimated WSS values was beyond the scope of this study.

6.5 Conclusion

In this study, we showed that the hemodynamic parameters such as mean flow, peak flow, flow waveform, WSS and OSI are influenced by spatial and temporal resolution of PC MRI measurements but to different extents. The mean flow is dependent on the spatial resolution which is caused by the segmentation errors. However, the effect of spatial resolution on the mean flow is small. We show that both mean flow and mean WSS are independent of temporal resolution. WSS is more sensitive to spatial resolution, while OSI is sensitive to both spatial and temporal resolution. Nevertheless, this study shows that the magnitude of mean and peak flow, WSS and OSI as well as the location of low and high WSS did not exhibit a strong dependency on the spatiotemporal resolution of the measurement.


