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Chapter 9

Aortic wall shear stress calculations using variable venc 4D flow MRI

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9.1 Introduction

Wall shear stress (WSS) is the tangential force exerted by the flowing blood on the vessel wall. WSS has been correlated with endothelial function and wall thickness (1). Quantification of WSS from 4D flow MRI is possible in the aorta (2–4), but is challenging in the diastolic phase of the heart cycle due to the presence of a relatively low velocity to noise ratio in diastole. In a recent paper, it was shown in software simulations that the presence of noise deteriorates the precision of WSS estimation, especially at lower shear rates (5). The availability of WSS data both in systole and diastole is important for the determination of the oscillatory shear index (6), and the transverse WSS (7).

The velocity noise in 4D flow MRI scales linearly with the phase of the signal and is thus inversely proportional to the encoding velocity (venc). One could thus in theory decrease the velocity noise by lowering the venc. However, this will induce multiple phase wraps in systole. Multi-venc techniques account for this by measuring multiple datasets with a different venc. Although the techniques appear to be more accurate, they do increase scan time (8–11). Recently, Nilsson et al. presented a method to vary the venc throughout the heart cycle in 4D flow MRI scans (vPC) (12) and showed that a dynamic variation of venc over the heart cycle significantly reduces noise levels in local velocity during diastole without phase wraps in systole.

Here we hypothesize that the use of variable venc 4D flow MRI will also benefit the quality of WSS data in diastole. If the velocities used for WSS determination become less noisy, the gradient close to the wall can be determined more reliably. Therefore, our aim was to investigate whether the use of a variable venc will translate in reduced noise levels in diastolic wall shear stress (WSS) quantification.

9.2 Materials and methods

9.2.1 Subjects and MRI

The aortas of 7 volunteers (age 27.5 ± 2.2 year, 5 males) were scanned using both a 4D flow MRI sequence with both a static encoding velocity (4D PC) and a variable encoding velocity (4D vPC). Approval for this research was granted by the institutional Ethics Committee. All participants provided written informed consent. Data were acquired on a 3 T MRI scanner (Ingenia, Philips Healthcare, Best, the Netherlands, software version 4.1.3) using two 16-channel phased-array coils, positioned at the anterior and posterior side of the volunteer. Scan parameters were similar to those used in (12): TE/TR/FA: 3.5 ms/ 8 ms/ 8°, non-interpolated spatial resolution 1.5–1.7 × 1.5–1.7 × 2.0 mm, temporal resolution 64 ms. The static venc for the 4D PC acquisition was determined for each volunteer, and ranged between 150 – 200 cm/s (median 160 cm/s). The dynamic venc for the 4D vPC acquisition varied between 50 cm/s in diastole and 184 cm/s in systole. The scheme for venc variation in the 4D vPC was determined for each volunteer, as described in (12). In short, three 2D PC MRI (3 times 57 seconds) of the aorta were made with using a venc of 200 cm/s in three orthogonal directions, to determine the cardiac-resolved peak velocities. These peak velocities were then automatically converted to the required venc values in the 4D vPC sequence. Prospective cardiac triggering was performed based on the ECG. No correction for the respiratory motion was made. In order to maintain equal TE, TR and resolution...
between the two acquisitions, the bandwidth for 4D vPC (345 Hz/pixel) was higher than the 4D PC bandwidth (248 Hz/pixel), theoretically decreasing the SNR in the 4D vPC acquisitions by 15%. Phase difference images were automatically corrected for static phase offset errors on the MR scanner console and manually corrected for phase wraps if needed. For the analysis, systole was defined as the three consecutive time points with maximum flow and diastole was defined as the three consecutive end-diastolic time points.

Figure 9.1: a velocity in the feet-head direction in the diastolic phase contrast images of the 4D PC scan (left) and the 4D vPC scan (right). b Location of the back muscle region used for noise quantification (red area). c Noise quantification results. The dots on the left represent the individual volunteer measurements; the bars represent the average noise level ± standard deviation (SD).

9.2.2 Flow quantification

We quantified time-resolved flow rates using GTFlow 2.1.4 (Gyrotools, Zurich, Switzerland) in the ascending and descending aorta and performed a Bland-Altman analysis to compare the absolute flow rates, for a full cardiac cycle, between 4D PC and 4D vPC datasets.

9.2.3 Velocity noise quantification

Noise levels in the velocity images were determined using the method described in (12). In short, we selected a region in static muscle tissue close to the aorta (see Figure 9.1 b) and calculated
9.2.4 Wall shear stress calculation

WSS was calculated as previously (13, 14). In short: at each location on the vessel wall, we fitted a smoothing spline to three velocity vectors, equally spaced along a 1 cm inward normal. The velocity at the vessel wall was forced to zero. We manually segmented the aortic lumen in both the PC and vPC scans using the average systolic image (using three peak-systolic time points) using ITK-SNAP (15). Side branches, proximal ascending aorta and the distal descending aorta were excluded from the segmentation. To compare WSS in 4D PC and 4D vPC data, we quantified mean aortic WSS in the ascending aortic arch, descending aortic arch and descending aorta separately. The average WSS results from 4D PC and 4D vPC for the entire aorta were compared using Bland-Altman analysis. P values of < 0.05 were considered statistically significant. To quantify the difference in WSS noise levels in the 4D PC and 4D vPC data for systole and diastole, the WSS variation was analyzed using 2D WSS maps of cut-open aorta segmentations. The Vascular Modeling Toolkit (VMTK version 1.2, www.vmtk.org) was used to cut open the vessels in a standardized fashion, after which 2D WSS magnitude maps were created in both systole and diastole (Figure 9.2). The distance along the centerline and the circumferential angle was used to project the original aorta WSS on a 2D WSS map.

The WSS map has no static region that would allow calculation of the noise levels based on standard deviation. We, therefore, decided to use the local spatial variation as an approximation for the noise levels in these 2D WSS maps. We know from fluid dynamics that for the main portion of the (healthy) aorta, true WSS maps would be smooth without sudden changes. The local spatial variation [Pa/cm] was obtained from the WSS map by means of convolution with a forward-difference kernel. The kernel consisted of a Sobel operator multiplied with a Gaussian filter (σ = 1.5 mm, similar to the spatial resolution). The histogram of this WSS variation map is considered here as a surrogate of the true noise in the WSS map. The distribution of WSS variation of 4D PC data was compared to 4D vPC using Levene’s test, both in systole and diastole.
In systole, both PC and vPC were measured with an almost equal venc and their mean WSS is therefore expected to be similar. Thus, the two measurements can be used to assess WSS reproducibility in systole as a quality indicator of the current datasets. For this purpose, we calculated the repeatability index (RI) for the systolic, mean WSS. The RI is defined as 1.96 times the standard deviation of the paired differences between WSS of successive 4D vPC and 4D PC scans, divided by the mean WSS, and expressed as a percentage:

$$ RI = \frac{1.96 \cdot SD_{\text{diff}}}{\text{mean}} $$

(9.1)

9.3 Results

9.3.1 Flow quantification

The flow rates for the 4D PC images were on average 6% ± 10% lower than for the 4D vPC data. This difference was not significant (paired two-tailed student t-test). A Bland-Altman analysis of the flow quantification (Figure 9.3) also showed a bias in flow rates between 4D PC and 4D vPC of −5.6 ml/s with a wide 95% confidence interval from −26 mL/s to 15 mL/s.

Figure 9.3: Bland-Altman of absolute flow in ascending and descending aorta with a bias of −5.6 mL/s (limits of agreement: −26 to 15 mL/s).

9.3.2 Velocity noise quantification

Both visual inspection and velocity noise quantification (Figure 9.1) showed a lower velocity noise for the 4D vPC sequence both in systole (P = 0.03) and diastole (P < 0.01). The difference in velocity noise in systole was −0.26±0.24 cm/s and the difference for diastole was −0.46±0.23 cm/s.

9.3.3 Wall shear stress

The average WSS over the entire aorta for 4D PC was 1.33±0.35 Pa in systole and 0.20±0.09 Pa in diastole and for 4D vPC 1.29±0.30 Pa in systole and 0.20±0.10 Pa in diastole. No significant differences in WSS mean or standard deviation were observed between 4D PC and 4D vPC results, neither globally nor for separate aorta parts (Figure 9.4). There were also no significant differences for the WSS minimum, median and maximum (data not shown). Visually, however, a smoother
appearance of the WSS patterns on the vessel wall is observed for 4D vPC, which can be especially appreciated by looking at the directionality of WSS in diastole (Figure 9.5).

The histogram of the WSS variation maps (Figure 9.6) shows the distribution of WSS variation over the entire aorta. It shows that 4D vPC based WSS has lower WSS variation compared to 4D PC based WSS. The same phenomenon was observed in all individual volunteers (data not shown). Levenes test indicated a significant difference between the SDs of the WSS variation ($P < 0.01$) in each volunteer and for all the volunteers combined. Although the differences are subtle, the WSS variation maps do show a decrease in WSS variation in the 4D vPC WSS maps compared to the 4D PC WSS maps.

RI for the systolic WSS was 6.8% for the entire aorta, and 8.6%, 8.7% and 8.1% for the ascending, descending arch and the descending aorta respectively.

![Figure 9.4: a Systolic and b diastolic WSS results for all seven volunteers (mean and standard deviation). Data shown is the global WSS in the aorta (black) and the separate parts ascending arch (red), descending arch (green) and descending aorta (blue).](image)

### 9.4 Discussion

In this study, we confirmed that the use of a variable venc reduces noise and increases the spatial homogeneity of WSS in the aorta compared to standard static venc acquisitions. In addition, we found that systolic and diastolic WSS can be calculated using both 4D PC and 4D vPC, yielding...
Figure 9.5: Typical example of a systolic and diastolic vectorial WSS map. a Systolic WSS based on 4D PC data. b Systolic WSS based on 4D vPC data. c Diastolic WSS based on 4D vPC data. d Diastolic WSS based on 4D vPC data.

WSS patterns that appear very similar to existing literature (5).

Figure 9.6: a Example WSS variation maps from 1 volunteer. From left to right: systole 4D PC, systole 4D vPC, diastole 4D PC, diastole 4D vPC. The colors depict low (blue) to high (red) local variations in WSS. b Combined histogram of 2D WSS variation map values for all volunteers. Low values on the x-axis indicate low noise. High values indicate high WSS variation. The red lines show the systolic data and the blue lines show the diastolic data.

We found that velocity noise quantification improved in vPC compared to PC for both systole and diastole. This can be explained by the automatically determined venc, which was lower in the vPC case, both for systole and diastole.

The average systolic and diastolic WSS magnitude was higher in this study than in existing literature (2, 3, 16), which can be explained by our higher spatial resolution combined with a slightly tighter segmentation of the aorta. We found no significant differences in the mean systolic and diastolic WSS between 4D PC and 4D vPC. The RI is in agreement with the recent paper on WSS reproducibility using the same WSS calculation method (17).

Despite a smoother visual appearance of the WSS from 4D vPC data, especially in the ascending aorta and aortic arch, the decrease in velocity noise did not result in a decrease of standard deviation in the derived WSS. This suggests that WSS distribution across the aorta is influenced by other factors as well. Such factors could, for example, be the presence of flow impingement zones, diameter differences along the aorta, velocity vortices, segmentation errors and the lack of breathing motion correction. (5).

Although no differences were found between PC WSS and vPC WSS in magnitude and standard deviation, the histograms of the WSS local variation maps that were tailored to show small-scale WSS differences did show significant differences in all volunteers. The WSS maps based on 4D vPC
scans contain relatively less spatial WSS variations, indicating the presence of less noise in WSS maps when using 4D vPC data as compared to 4D PC data. One explanation for the relatively small differences observed here is that the WSS algorithm, which uses smoothing splines, already filters the velocity noise, such that the effect of velocity noise is dampened (5).

This work suffers from some limitations. Due to the difficulty of accurate segmentation from the diastolic data, we used systolic segmentations also for diastole. This may have induced WSS errors, especially near the aortic root in diastole. Furthermore, the increased bandwidth for the 4D vPC scan will have limited (±15%) the velocity to noise gain of the 4D vPC sequence, dampening the hypothesized effect. However, the choice of a fixed TE, TR and resolution was made to avoid those confounding factors in the comparison. TE and TR were fixed to obtain a similar signal, whereas the resolution was mainly fixed to avoid differences in WSS quantification (2–4).

In conclusion, we have shown that WSS can be derived using both 4D vPC and 4D PC data. The decrease in noise in 4D vPC gives a smoother WSS map, but the improvement is small, suggesting that other factors than the quality of the velocity data also influences WSS variations. The present results highlight the small yet significant benefit of variable velocity encoding beyond decreasing the noise occurring in the velocity data itself.

Bibliography


