Quantitative 2D and 3D Phase Contrast MRI: Optimized Analysis of Blood Flow and Vessel Wall Parameters

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Abstract:
Quantification of CINE phase contrast (PC)-MRI data is a challenging task because of the limited spatio-temporal resolution and signal-to-noise ratio. The method presented in this paper combines B-spline interpolation and Green’s theorem to provide optimized quantification of blood flow and vessel wall parameters. The B-spline model provided optimal derivatives of the measured 3-directional blood velocities onto the vessel contour as required for vectorial Wall Shear Stress (WSS) computation. Eight planes distributed along the entire thoracic aorta were evaluated in a 19-volunteers study using both high spatio-temporal resolution planar 2D-CINE-PC (~1.4x1.4mm²/24.4ms) and lower resolution 3D-CINE-PC (~2.8x1.6x3mm³/48.6ms) with 3-directional velocity encoding. Synthetic data, error propagation, inter-individual, inter-modality and inter-observer variability were used to evaluate the reliability and reproducibility of the method. While the impact of MR measurement noise was only minor, limited resolution of PC-MRI introduced systematic WSS underestimations. In-vivo data demonstrated close agreement for flow and WSS between 2D and 3D-CINE-PC as well as observers and confirmed the reliability of the method. WSS analysis along the aorta revealed the presence of a circumferential WSS component accounting for 10-20%. Initial results in a patient with atherosclerosis suggest a potential of the method to understand the formation and progression of cardiovascular diseases.

Keywords: phase-contrast MRI (PC-MRI), wall shear stress (WSS), flow quantification, B-spline, Aorta hemodynamics.
Introduction:
The functional evaluation of the cardiovascular system is already part of the clinical routine and is expected to gain increased importance (1). Volumetric blood flow is an important estimator of the cardiovascular function in presence of stenosis, aortic regurgitation (2) or congenital defects (3). In addition, the measurement of local flow profiles can provide important derived flow or vessel wall parameters such as pressure difference, peak velocity, pulsatility index and wall shear stress (WSS). WSS, the friction force of the flowing blood at the arterial wall, affects the function of endothelial cells (4-6), the development of atherosclerosis (4, 7-10) and aneurysmal development (11).

To assess cardiovascular function in-vivo, blood flow velocity can be measured using Doppler ultrasound or flow-sensitive MRI. Although Doppler ultrasound offers high spatio-temporal resolution, it is hampered by its user-dependency, limited insonation angles (12) and unidirectional velocity encoding. The intrinsic sensitivity of MR to flow offers the possibility to analyze vascular hemodynamics without restrictions to anatomic coverage or flow directions.

In this context, an alternative approach is provided by computational fluid dynamics (CFD) models with realistic boundary conditions (i.e. vascular geometry and inflow provided by CT, MRI or ultrasounds) and has already been used (11, 13-15). However, it is still debated how restricting assumptions on blood rheology, vessel properties or blood-vessel interactions may affect the accuracy of the results.

WSS depends on the spatial velocity gradient at the vessel wall and can therefore be calculated from the measured velocity fields. Considering the 3-dimensional nature of blood flow, WSS is a vector quantity ($\tau$) that can be expressed in N/m$^2$. However, deriving WSS from the discrete PC-MR velocity data remains challenging. Limited spatial resolution, partial volume effects and numerical derivation of the velocity field are likely to introduce underestimations in WSS. Nevertheless, the definition of suitable WSS estimators of WSS patterns is of high interest. Although WSS may systematically be underestimated, results may still be sufficient to characterize normal and pathological spatio-temporal variations of WSS. Note that in this paper, the term WSS is used to describe WSS estimations based on the interpolation of local velocity derivatives.

Although previous in-vivo MR studies provided insights into the relationship between WSS and flow (10, 16, 17), the reported WSS were limited to the mean axial WSS, i.e. projection of the WSS vector along the lumen direction. No comprehensive or circumferential assessment of localized WSS vector components along the vessel wall has been presented to date. WSS estimations are often simply calculated assuming a global axial parabolic velocity profile. The WSS ($\tau$) is then oriented along the axial direction only and WSS simplifies to: $\tau = \frac{4\eta Q}{\pi a^3}$. (with $a =$ vessel radius, $Q =$ flow and $\eta =$ dynamic viscosity). However, this simplification is only valid for constant laminar flow in a straight tube.

In the 3D paraboloid method (18), axial parabolic flow profiles were assumed in sectors near the vessel wall in order to compute axial WSS. The method required only minor user input and presented excellent repeatability but its applicability was restricted to small or medium sized elliptical vessels by its assumption of axial-only and paraboloid flow (19). Recently, a more
general method based on Lagrange polynomial interpolation of through-plane MR velocities was introduced to compute axial WSS for large arteries (20).

However, it has been shown that even flow in medium sized vessels of healthy volunteers can present more complex flow with secondary patterns such as helical flow (21). In larger arteries or in presence of cardiovascular diseases, blood flow can be severely altered and can thus differ even more from an ideal parabolic profile (22-24). In addition, even in the presence of limited secondary flow velocities, the influence on WSS can be important (25). Consequently, the axial component of WSS, which was typically used in most studies, may not be sufficient to fully estimate the impact of the 3-directional blood flow on the vessel wall. For complex flow, the vectorial time-resolved WSS needs to be considered.

*In-vivo* WSS vector measurements at specific points were already reported in the aorta and the carotid bifurcation using simple linear near-wall velocity profile assumptions (26). However, those measurements did not allow computing WSS in complete arterial sections which were to date only reported based on *in-vitro* models with idealized boundary conditions (13,14).

Recent reports indicate the potential of 3D CINE phase contrast MRI (flow sensitive 4D-MRI) for the detailed visualization of complex flow patterns associated with healthy and pathologic hemodynamics (24,27). The nature of such datasets (3 spatial dimensions, 3 blood flow velocity directions and time) points towards the potential of flow-sensitive 4D MRI to provide detailed quantitative flow and vessel wall parameters with complete vascular coverage.

The purpose of this work was to take full advantage of the 3-directional nature of MR data and develop an optimized quantitative analysis method to derive vectorial flow and wall parameters from CINE phase contrast (PC) MR data. The data analysis strategy combines Green’s theorem and B-spline interpolation with their finite difference property to provide an optimal quantification of several blood flow and vessel wall parameters. Calculation of the local blood flow velocity derivatives on the vessel contour using B-spline interpolation allows a direct estimate of time-resolved segmental WSS vectors independent of any global assumptions regarding the flow profile.

To our knowledge, the methods and results presented in this study constitute the first report of *in-vivo* analysis of blood flow parameters and vectorial WSS over complete arterial sections. To test the accuracy of the proposed quantification strategy, synthetic flow data and error propagation analysis were used to evaluate the influence of spatial resolution and signal-to-noise ratio (SNR). To further investigate the effect of spatial and temporal resolution, a detailed comparison of high resolution 2D CINE PC with lower resolution 3D CINE PC data was performed in 19 healthy volunteers *in-vivo*. The aim was to investigate the performance of our data processing strategy and its reliability for analyzing CINE 3D PC data compared to a spatially registered 2D PC technique.

**Materials and Methods:**

**Synthetic data**

Synthetic datasets were created using a parabolic flow profile with mean velocity of 0.5m/s in a vessel of diameter 30mm. According to the Poiseuille’s flow equation, this results in a flow volume of 353mL/s and a homogeneous axial WSS of 0.6N/m². The initial high-resolution synthetic dataset with an isotropic pixel size of 0.15x0.15mm² was reduced in 40 steps in order
to evaluate the robustness of the quantification method. Filtering with a MRI point-spread function (point-spread due to truncation, (28)) simulated increasing pixel size (i.e. isotropic resolution reduction) and Gaussian filtering represented the effects of increased smoothing. The vessel lumen was manually segmented and identical segmentation contours were used for all levels of resolutions and smoothing.

**In-vivo MR acquisitions**

Flow measurements were performed in the thoracic aorta of 19 healthy volunteers (mean age 23 years, range: 20-34, 4 females). Data were acquired on a 3T MR system (Magnetom TRIO, Siemens, Germany, Gmax=40mT/m, rise time=200μsec, 8-channel receive coil) using an rf-spoiled gradient echo sequence during free breathing and prospective ECG gating. Respiration control was performed based on combined adaptive k-space reordering and navigator gating (27).

Data were acquired with interleaved 3-directional velocity encoding at 8 2D planes (2D-CINE-3dir.PC) transecting the thoracic aorta and in a 3D volume (3D-CINE-3dir.PC) covering the complete thoracic aorta. The 2D planes were positioned at precise landmark locations along the thoracic aorta as schematically illustrated in Fig. 1 (left). The pulse sequence parameters for both 2D and 3D acquisitions are summarized in Table 1 and correspond to commonly used parameters for 3D blood flow visualization (27).

**Table 1: Sequence parameters for in-vivo acquisitions**

<table>
<thead>
<tr>
<th></th>
<th>2D-CINE-3dir.PC</th>
<th>3D-CINE-3dir.PC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voxel size [mm³]</td>
<td>1.24-1.82 x 1.25-1.82 x 5</td>
<td>2.71-2.93 x 1.58-1.69 x 2.60-3.5</td>
</tr>
<tr>
<td>(average between volunteers)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temporal resolution [ms]</td>
<td>4TR = 24.4</td>
<td>8TR = 48.8</td>
</tr>
<tr>
<td>$v_{enc}$ [cm/s]</td>
<td>150</td>
<td>150</td>
</tr>
<tr>
<td>TE / TR [ms]</td>
<td>3.57 / 6.1</td>
<td>3.67 / 6.1</td>
</tr>
<tr>
<td>Bandwidth [Hz/pixel]</td>
<td>455</td>
<td>480</td>
</tr>
<tr>
<td>$\alpha$ [°]</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Acquisition time [min]</td>
<td>2-5</td>
<td>10-20</td>
</tr>
<tr>
<td>Number of time frames</td>
<td>28-40</td>
<td>13-15</td>
</tr>
</tbody>
</table>

For each cine time frame, the velocity encodings for the four acquisitions (reference and three velocity-sensitive scans) were executed consecutively for 1 and 2 k-space lines along the phase-encoding direction in 2D and 3D, respectively. This resulted in a temporal resolution of 4TR in 2D and 8TR in 3D. (27). After acquisition, data were corrected for eddy currents, i.e. correction of the linear phase drift according to the static tissues phase drift (29). In a few cases, velocity aliasing was corrected based on an automatic algorithm and manual screening (30).

In addition, a patient (female, age 48 years) hospitalized in the stroke unit of our institution with acute brain ischemia was examined using the 3D-CINE-3dir.PC protocol. Atherosclerosis and a complex plaque in the descending aorta were demonstrated by a previously reported high-resolution 3D MRI protocol (31).

The study was approved by the local ethics committee and written informed consent was obtained from all subjects.
Fig. 1: Schematic illustration of the location of the 8 flow analysis planes (left) and of the decomposition of the estimated wall shear stress into axial and circumferential components (right). The eight 2D planes are positioned in the ascending aorta (planes 1-3), aortic arch (planes 4-5) and the descending aorta (planes 6-8) with innermost curvature reference positions marked by black dots. WSS estimation is illustrated for the proximal descending aorta (plane 6): Reduced flow along the inner curvature results in asymmetric velocity profiles (dashed lines) and consequently different WSS vectors (gray arrows) at the vessel wall. Note that WSS is a vector quantity and that complex flow including helical flow components can induce shear forces along the lumen circumference (circ. WSS) in addition to WSS along the main flow direction (axial WSS).

Data analysis
The data processing strategy is illustrated in Fig. 1 and 2. Analysis planes at eight locations in the thoracic aorta (Fig. 1, left) were either taken from the image orientation of 2D imaging (2D-CINE-3dir.PC, Fig. 2, top left) or retrospectively extracted from the 3D data (3D-CINE-3dir.PC, Fig. 2, top right). For 3D-CINE-3dir.PC analysis planes were extracted within the 3D data volume at the exact location of the 2D imaging planes using a 3D visualization software (Ensight, CEI, Apex NC, USA) (32). The resulting planar magnitude data and three-directional velocities were imported into an in-house analysis tool based on Matlab (MathWorks, USA) which allowed for segmentation and data analysis (33,34). For each dataset, several flow and wall parameters were derived: area, flow, time to peak flow, vectorial wall shear stress and oscillatory shear index (OSI). In order to compensate for small local fluctuations due to noise, data were filtered with a Gaussian low-pass filter of fixed radius (1 mm).
**Segmenation and registration**

For each CINE time frame the vessel lumen was segmented using cubic B-splines. All segmentation tasks were integrated into a graphical user interface which allowed for interactive frame-wise segmentation by adjusting the position of the interpolating knots, i.e. a finite numbers of points on the contour (Fig. 2, mid). The interpolating knots positions were subsequently used to derive the control points \((c_{x,k}, c_{y,k})\) defining the spline. The actual lumen contour \((x(t), y(t))\) and its derivatives \((\dot{x}(t), \dot{y}(t))\) could then be analytically calculated in parametric form (parameter = t) according to the B-spline definition (see Appendix A for details):

\[
x(t) = \sum_{k \in \mathbb{Z}} c_{x,k} \beta^3(t-k) \tag{1}
\]

\[
y(t) = \sum_{k \in \mathbb{Z}} c_{y,k} \beta^3(t-k) \tag{2}
\]

\[
\dot{x}(t) = \sum_{k \in \mathbb{Z}} c_{x,k} \frac{\partial \beta^3}{\partial t}(t-k) \tag{2}
\]

\[
\dot{y}(t) = \sum_{k \in \mathbb{Z}} c_{y,k} \frac{\partial \beta^3}{\partial t}(t-k) \tag{2}
\]

Where \(\beta^3\) is the cubic B-spline basis function of 3rd order and
\[
\frac{\partial \beta^3}{\partial t} \quad \text{represents the cubic differential B-spline basis function of 3rd order.}
\]

Note that the control points \((c_{x,k}, c_{y,k})\) do not belong to the contour and were calculated from the interpolating knots in order to facilitate the segmentation procedure. A fundamental property of B-spline defines \(\frac{\partial \beta^3}{\partial t}\) as a finite difference (Eq. [A2]), hence permitting the analytical calculation of [2].

A reference point corresponding to the inner curvature of the aorta was defined on every contour (black dots on Fig. 1 and 9) in order to allow spatial registration of the WSS vectors between the 2D-CINE-3dir.PC and 3D-CINE-3dir.PC acquisitions.

**Interpolation of MR-velocities**

To compensate for the limited spatial resolution of the PC MR data, cubic B-spline interpolation was used. Similarly to the B-spline model used for segmentation, the B-spline interpolation model provided continuous velocity and derivatives on the vessel contour. Due to the finite difference property of B-splines, the analytical derivatives, i.e. local velocity gradient along the segmentation contour \(\partial D\) could be efficiently and easily calculated by using another basis function. (Appendix A)

**Numerical computation of WSS**

The WSS vector \(\tau\) for a Newtonian incompressible fluid can be derived from the velocity field based on the deformation tensor at the vessel wall (Appendix B):

\[
\tau = 2\eta \hat{\epsilon} \cdot \hat{n}
\]

with \(\eta\) : viscosity, \(\hat{n}\) : inward unit normal and the deformation tensor:

\[
\hat{\epsilon}_{ij} = \frac{1}{2} \left( \frac{\partial v_i}{\partial x_j} + \frac{\partial v_j}{\partial x_i} \right)
\]

\(\hat{\epsilon}_{ij}\) is directly related to the local velocity derivatives at the vessel lumen, i.e. on the segmentation contour \((i,j = [1,2,3] = 3\) orthogonal coordinates, \(v = \) velocity components, \(x = \) the spatial dimensions).

Calculation of the deformation tensor (Eq. [4]) required the 3-dimensional derivation of the velocity vector field. However, assuming transversal 2D analysis planes and no flow through the vessel wall, Eq. [3] can be simplified to calculate 3D WSS vectors from 2D planes with 3-directional velocity fields (Appendix C).

In order to ensure that the estimated WSS vector is tangential to the vessel wall, the projection of \(\tau\) on the tangential plane was used for the measured WSS (14):

\[
\tau_{\exp} = \hat{n} \times \left( \tau \times \hat{n} \right)
\]

The WSS vector can be separated into its axial and circumferential components as shown in Fig. 1 (right). In this paper we use WSS to denote the magnitude of the WSS vector.
The velocity derivatives \( \frac{\partial v_j}{\partial x_i} \) were calculated on the vessel contour using the cubic B-spline interpolation model which provides first order analytical derivatives. Eq. [5] was evaluated for each CINE timeframe with 256 points along the segmented lumen contour. The inward unit normal vector \( \vec{n} \) along the lumen contour was analytically calculated from the cubic B-spline contour of the vessel. For each time frame, average WSS vectors were calculated for 12 angular segments along the lumen circumference starting at the reference point at the inner aortic curvature. A dynamic viscosity \( \eta \) of 4.5 cP was assumed (35).

**Numerical computation of OSI**

The oscillatory shear index (OSI) represents the temporal oscillation of WSS during the cardiac cycle. It was originally defined by Ku et al (8), and was further adapted to a general three-dimensional case by He and Ku (36). In this study, the second definition (36) was used:

\[
OSI = \frac{1}{2} \left( 1 - \frac{\int_0^T \tau \cdot dt}{\int_0^T |\tau| \cdot dt} \right) \tag{6}
\]

Where \( T \) is the duration of the cardiac cycle and \( \vec{\tau} \) is the instantaneous wall shear stress vector. The oscillatory shear index in Eq. [6] was numerically computed from the \( \vec{\tau} \) after temporal resampling using cubic B-spline temporal interpolation. A 20-fold temporal resampling was found to be sufficient and used for this study.

**Integration using Green’s theorem**

Using Green’s theorem (Appendix D), surface integrals can be simplified to contour integrals. This considerably simplifies the practical implementation of 2-dimensional integration with interpolation, while limiting the computational burden and the numerical error. The lumen contour \( \partial D \), Fig. 2) being defined parametrically by \( (x(t), y(t)) \), area and flow calculations over the lumen surface \( D \) can then be simplified to computing single integrals along \( \partial D \):

\[
A = \left| \oint_{\partial D} (x(t)\dot{y}(t) - y(t)\dot{x}(t)) dt \right| \tag{7}
\]

\[
|\text{Flow}| = \left| \oint_{\partial D} P \nu^3_y (x(t), y(t)) \dot{x}(t) dt \right| \tag{8}
\]

With: \( P \nu^3_y (x, y) = \int_{-\infty}^{y} \nu^3_y (x, y_N) dy_N \) \tag{9}

Where \( \nu_y \) is the through-plane velocity

The numerical integration of Eq. [9] was carried out at the original resolution (size \( N \)) while Eq. [7] and [8] were integrated using interpolation on \( \partial D \) (size \( N_i \)). The computational complexity for the area and flow calculations were thus reduced to \( O(N) \) and \( O(N_i \cdot N) \), respectively compared to \( O(N_i^2) \) with the same oversampling factor but using a surface integral. \( N_i = 256 \) was typically used.
Validation

Inter-observer and inter-modality variability

The 2D and 3D data of the first analysis plane of 8 volunteers were independently segmented by a second observer and all derived flow and wall parameters were compared. Inter-observer and inter-modality (2D vs. 3D acquisitions) variability were evaluated by calculating relative and absolute errors: $E_{rel} = \frac{2|m1-m2|}{|m1+m2|}$ and $E_{abs} = |m1-m2|$, m1 and m2 being the two independent measurements. The errors of the total flow per cardiac cycle and the mean vessel area during one cardiac cycle were assessed based on all analysis planes. The errors of the mean WSS during one cardiac cycle and of the OSI were evaluated based on all analysis planes and all WSS segments.

Error Propagation Analysis

Velocity data

To evaluate the influence of SNR of the PC-MRI raw data on the derived flow and wall parameters, a detailed analysis of error propagation was performed. Based on the mean SNR measured in the aorta of all volunteers and all planes, noise in the velocity images was estimated according to (37):

$$\sigma_v = \frac{\sqrt{2} v_{enc}}{\pi SNR}$$

Where $SNR$ is the measured magnitude signal to noise ratio based on the signal magnitude within the lumen and the background noise, $v_{enc}$ is the velocity sensitivity.

B-spline interpolation

Based on Eq. [A4], the 1D cubic B-spline derivative kernel produces a propagation of error with a factor:

$$a_{B-spline} = \sqrt{\sum_{k \in Z} \left( \frac{\partial f_k}{\partial x} (x-k) \right)^2 \frac{1}{\Delta l}}$$

Where $\frac{\partial f_k}{\partial x}$ is given by Eq. [A6] and $\Delta l$ is the sampling period.

Spatio-temporal averaging

Finally, spatial and temporal averaging affects the error propagations with factors

$$a_{contour} = \frac{\Delta l}{\text{circumference}}$$
$$a_{lumen} = \sqrt{\frac{\Delta l^2}{\text{area}}}$$
$$a_{time} = \frac{1}{\text{number of timeframes}}$$

over the lumen contour, over the lumen area and over the cardiac cycle.

Flow and WSS

The error propagation on the flow volume is given by:

$$\sigma_{flow} = area \cdot \sigma_v \cdot a_{lumen} \cdot a_{time}$$
Simplifying the B-spline interpolation to one dimension, the error propagation for the wall shear stress averaged over the lumen contour and the cardiac cycle is given by:

$$\sigma_{WSS} = \mu \cdot \sigma_v \cdot a_{B-spline} \cdot a_{contour} \cdot a_{time}$$  \[13\]

**Results:**

**Synthetic data**

The effect of systematically varied spatial resolution and low-pass filtering amplitudes on the calculation of flow and WSS for synthetic data is shown in Fig. 3. Since low-pass filtering (A) is similar to a decrease in spatial resolution (B), both graphs present very similar shapes. It is evident that the proposed method can calculate the almost exact flow and WSS for ideal conditions, i.e. small voxel size and no smoothing. Low resolution strongly affects WSS while the total flow remains relatively constant. Even at relatively high resolution, WSS is markedly reduced, e.g. for a voxel length of 1mm the WSS is reduced to 60% of its original value. For further increasing voxel length, WSS remains more stable and is still above 30% of its original value for a voxel length of 10mm. In contrast, low-resolution imaging introduces very little flow underestimations. The average pixel length and the smoothing radius used in our study are represented by the dashed vertical lines. A 1mm smoothing and the resolutions used in this study would limit the WSS estimation to about 50% of its real value.

**Fig. 3:** Effect of Gaussian prefiltering (A) and pixel size (B) on derived flow and WSS for a parabolic synthetic flow profile (mean velocity 0.5 m/s, diameter 30 mm, flow 353 mL/s, WSS 0.6 N/m²). The horizontal lines correspond to the theoretical values of flow and WSS. The prefiltering settings and pixel size used in the volunteer study are indicated by the vertical lines.
In-vivo data

Volunteer study

Flow quantification in the aorta

Exemplary results of time-resolved blood flow based on 2D and 3D PC-MRI and averaged over all 19 volunteers are shown in Fig. 4.

![Fig. 4: Average time-resolved volumetric blood flow in the aorta calculated from 2D-CINE-3dir.PC and 3D-CINE-3dir.PC data for all 19 volunteers. Temporal evolution of blood flow during the cardiac cycle in the ascending aorta (left, planes 1, 3) and descending aorta (right, planes 6, 8) demonstrated close agreement between both methods. Note that systolic peak velocities and early diastolic retrograde flow were underestimated for 3D data. The error bars represent the standard deviation over all volunteers.](image)

The small standard deviations reflecting inter-individual differences between volunteers indicate the high consistency of normal blood flow in young normal subjects. This is coherent with peak aortic velocities previously reported in healthy volunteers (24). As expected, flow quantification based on 3D data slightly underestimated peak systolic and early diastolic retrograde flow. Nevertheless, the flow quantification over all volunteers demonstrated close agreement between 2D and 3D acquisitions as summarized in table 2.

Volumetric blood flow remained constant in the ascending aorta (planes 1-3) and decreased progressively in the aortic arch as blood is flowing into the supra-aortic arteries. In the descending aorta (planes 6-8), the flow changes were again limited. Time to peak flow was slightly but systematically overestimated by the 3D data. As a consequence of the compliance of the aorta, the time to peak flow progressively increased along the aorta.

The absolute errors and absolute relative errors between 2D-CINE-3dir.PC and 3D-CINE-3dir.PC for all evaluated flow parameters, i.e. the effect of spatiotemporal-resolution on flow quantification, are shown in Table 3 and Fig. 5. The median relative errors of flow and area remained below 18% in 2D and 3D.
Table 2: In-vivo quantification of blood flow and vessel wall parameters in the aorta. All data are presented as average values over 19 volunteers. The standard deviation between volunteers is given in brackets.

**Table 2A: Results from 2D-CINE-3dir.PC data.**

<table>
<thead>
<tr>
<th>Plane:</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flow [mL/cycle]</td>
<td>74.4</td>
<td>70.2</td>
<td>70.7</td>
<td>51.8</td>
<td>48.7</td>
<td>50.0</td>
<td>61.6</td>
<td>63.8</td>
</tr>
<tr>
<td>Area [mm²]</td>
<td>527</td>
<td>489</td>
<td>454</td>
<td>402</td>
<td>363</td>
<td>311</td>
<td>317</td>
<td>295</td>
</tr>
<tr>
<td>Mean Vel. [m/s]</td>
<td>0.183</td>
<td>0.187</td>
<td>0.203</td>
<td>0.168</td>
<td>0.170</td>
<td>0.211</td>
<td>0.250</td>
<td>0.278</td>
</tr>
<tr>
<td>Time to peak [ms]</td>
<td>99.6</td>
<td>100</td>
<td>102</td>
<td>116</td>
<td>122</td>
<td>175</td>
<td>174</td>
<td>166</td>
</tr>
<tr>
<td>Mean WSS [N/m²]</td>
<td>0.431</td>
<td>0.447</td>
<td>0.444</td>
<td>0.385</td>
<td>0.414</td>
<td>0.466</td>
<td>0.530</td>
<td>0.564</td>
</tr>
<tr>
<td>Circ. WSS [%]</td>
<td>11.8</td>
<td>15.7</td>
<td>16.2</td>
<td>19.4</td>
<td>18.6</td>
<td>10.9</td>
<td>12.1</td>
<td>14.4</td>
</tr>
<tr>
<td>OSI mean [%]</td>
<td>6.55</td>
<td>5.29</td>
<td>5.12</td>
<td>5.94</td>
<td>7.47</td>
<td>7.68</td>
<td>8.42</td>
<td>7.49</td>
</tr>
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</table>

**Table 2B: Results from 3D-CINE-3dir.PC data.**

<table>
<thead>
<tr>
<th>Plane:</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flow [mL/cycle]</td>
<td>73.9</td>
<td>67.0</td>
<td>63.8</td>
<td>50.8</td>
<td>48.4</td>
<td>44.2</td>
<td>45.4</td>
<td>48.5</td>
</tr>
<tr>
<td>Area [mm²]</td>
<td>506</td>
<td>451</td>
<td>435</td>
<td>368</td>
<td>355</td>
<td>317</td>
<td>300</td>
<td>269</td>
</tr>
<tr>
<td>Mean Vel. [m/s]</td>
<td>0.224</td>
<td>0.229</td>
<td>0.226</td>
<td>0.207</td>
<td>0.204</td>
<td>0.211</td>
<td>0.228</td>
<td>0.270</td>
</tr>
<tr>
<td>Time to peak [ms]</td>
<td>119</td>
<td>119</td>
<td>123</td>
<td>139</td>
<td>139</td>
<td>171</td>
<td>174</td>
<td>179</td>
</tr>
<tr>
<td>Mean WSS [N/m²]</td>
<td>0.294</td>
<td>0.309</td>
<td>0.306</td>
<td>0.311</td>
<td>0.308</td>
<td>0.308</td>
<td>0.317</td>
<td>0.384</td>
</tr>
<tr>
<td>Circ. WSS [%]</td>
<td>24.4</td>
<td>24.9</td>
<td>23.9</td>
<td>25.4</td>
<td>25.8</td>
<td>26.8</td>
<td>26.8</td>
<td>17.4</td>
</tr>
<tr>
<td>OSI mean [%]</td>
<td>7.81</td>
<td>7.61</td>
<td>7.77</td>
<td>7.77</td>
<td>8.56</td>
<td>8.21</td>
<td>8.46</td>
<td>6.11</td>
</tr>
</tbody>
</table>

Table 3: Mean absolute errors between 2D-CINE-3dir.PC (2D) and 3D-CINE-3dir.PC (3D) as well as between observers in 2D and 3D. The standard deviation of the error between volunteers is given in brackets.

<table>
<thead>
<tr>
<th></th>
<th>2D vs. 3D</th>
<th>interobserver 2D</th>
<th>interobserver 3D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flow [mL/cycle]</td>
<td>8.88</td>
<td>1.61</td>
<td>2.69</td>
</tr>
<tr>
<td>Area [mm²]</td>
<td>36.8</td>
<td>32.3</td>
<td>44.7</td>
</tr>
<tr>
<td>Mean Vel. [m/s]</td>
<td>0.0387</td>
<td>0.00423</td>
<td>0.0053</td>
</tr>
<tr>
<td>Time to peak [ms]</td>
<td>17.7</td>
<td>7.73</td>
<td>7.17</td>
</tr>
<tr>
<td>Mean WSS[N/m²]</td>
<td>0.159</td>
<td>0.033</td>
<td>0.0477</td>
</tr>
<tr>
<td>OSI mean [%]</td>
<td>5.04</td>
<td>0.827</td>
<td>2.11</td>
</tr>
</tbody>
</table>
**WSS estimation in the aorta**

For the same analysis planes as in Fig. 4, exemplary results of the estimation of time-resolved WSS magnitude are depicted in Fig. 6 where the individual curves represent WSS magnitude averaged over the lumen contour and over all volunteers.

Findings of WSS estimation for all 8 analysis planes are summarized in table 2. The spatial (table 2) and temporal (Fig. 6) evolutions of WSS closely agreed between 2D-CINE-3dir.PC and 3D-CINE-3dir.PC data for all 19 volunteers. Temporal evolution of WSS magnitude during the cardiac cycle in the ascending aorta (left, planes 1, 3) and descending aorta (right, planes 6, 8) demonstrated similar shapes but a clear underestimation of WSS estimated from the 3D data. Note that the relatively small error bars represent inter-individual variations in WSS and thus indicate the high consistency of the derived WSS data in our group of young healthy volunteers.
3D-CINE-3dir.PC. However, 3D-CINE-3dir.PC, based on lower spatio-temporal resolution, systematically underestimated WSS magnitude as expected from the synthetic data analysis. Mean WSS magnitude showed minor increase along the aorta what correlates well with the evolution of the mean velocity. Note that the fraction of the circumferential component of the WSS vector was between 10% and 20% indicating that the vectorial nature of WSS has to be taken into account to fully characterize the wall shear forces. Processing of 3D data generally resulted in larger circumferential WSS components compared to 2D. Finally, the average OSI over all volunteers and WSS segments remained small (5 to 9%) for all analysis planes and was slightly higher for the 3D data. The median relative errors for WSS and OSI were within 45 and 65% respectively (Fig. 5). The absolute error of OSI remained yet limited at about 5% (Table 3). Those errors are larger than the error predicted from the synthetic data.

Fig. 7 shows the local evolution of WSS averaged over all volunteers as a function of analysis plane location, i.e. distribution along the thoracic aorta.

The standard deviations between volunteers, as represented by the error bars, remained relatively small for both 2D and 3D data. Axial WSS and WSS magnitude estimated from 2D acquisition increased slowly in the ascending aorta (planes 1-3), decreased near to the supra-aortic branches in the aortic arch (planes 4-5), and eventually increased again in the descending aorta (planes 6-8). Axial and magnitude WSS estimated from the 3D acquisition presented less variations but the WSS increase in the descending aorta is clearly recognizable. Quantitatively, axial and...
magnitude WSS, as calculated from the 3D data, were underestimated in comparison to the 2D data. The average circumferential WSS over all volunteers was positive (right-handed circumferential component) in the ascending branch of the aorta and inverted in the descending aorta (left-handed circumferential component). Interestingly, the distribution of circular WSS closely resembled known helical flow patterns in the thoracic aorta changing from right-handed helix in the upper aortic-arch (planes 1 to 4) to left-handed helix in the descending aorta (planes 5 to 8) (24). The circumferential WSS pattern was similar between the 2D and 3D measurements.

A more detailed analysis of the differences between 2D and 3D WSS estimations are provided in the Bland-Altman plots of the axial and circumferential components for all volunteers and analysis planes in Fig. 7 C-D. Axial WSS was smaller (on average by 0.078 N/m²) when estimated from 3D data in comparison to 2D data. In contrast, the circumferential WSS did not exhibit a significant systematic bias between 2D and 3D. The 2D-3D difference was smaller and almost symmetric between -0.07 and 0.07N/m².

**Inter-observer variability**

Fig. 8 illustrates the inter-observer variability based on repeated processing of the 2D (A) and 3D (B) data by 2 independent observers. Overall, variations were moderate with a median relative inter-observer error of approximately 8/17% in 2D/3D. The median inter-observer error for OSI was relatively large in proportion (up to 30% relative error in 3D) but the absolute error remained small (up to 2% in 3D, Table 3). The error introduced by lumen segmentation between the 2 observers was generally higher for the 3D data, i.e. lower resolution, compared to the 2D data at higher spatio-temporal resolution. Flow, area and WSS showed low median relative error and inter-quartile distances of the relative error indicating that the inter-observer error is relatively stable between measurements.

![Fig. 8: Boxplots of the absolute value of the inter-observer relative error for 2D-CINE-3dir.PC (A) and 3D-CINE-3dir.PC (B) for total flow, lumen area, mean velocity, time to peak flow, WSS magnitude and OSI. The statistics are based on values for all volunteers. Red line = median, blue box = lower and upper quartile values, dashed lines = most extreme values within 1.5 times the inter-quartile range from the ends of the box, red + sign = outliers, i.e. data with values beyond the ends of the whiskers.](image-url)
**Segmental WSS**

To illustrate the potential of the presented flow analysis strategy for detailed evaluation of the spatial distribution of WSS, Fig. 9 depicts time-averaged WSS vectors and OSI for one volunteer.

**Fig. 9:** Segmental distribution of temporally averaged WSS vectors and OSI in the ascending (planes 1, 3) and descending (planes 6, 8) aorta for a normal volunteer. WSS and OSI were extracted for 12 segments along the vessel circumference with the innermost curvature reference positions marked by black dots. For the representation, the OSI index for each WSS segment is scaled and opposed to the WSS magnitude, e.g. an OSI of 0.5 would be represented as a bar of the same length as the WSS vector but of opposed direction. For each analysis plane, a direct comparison of WSS vectors (green bars) and OSI (magenta bars) for 2D-CINE-3dir.PC (red planes) and 3D-CINE-3dir.PC (blue planes) is shown. Agreement of the segmental WSS and OSI distribution between both data acquisition methods is clearly visible. The expected underestimation of WSS by the lower resolution 3D data is particularly evident for the high WSS in the descending aorta (plane 8). Note that all planes illustrate the vector nature of WSS and include non negligible circumferential WSS components.

Although the major WSS components are axial, the vectorial aspect of WSS is clearly visible. In the ascending aorta (slice 1) and in the aortic arch (slice 3), the WSS vectors (green bars) present a substantial right-handed circumferential component in combination with higher OSI (magenta bars) on the inner-curvature of the aortic arch. In contrast, the WSS vectors in the descending aorta show a left-handed circumferential component. Note that the spatial distribution of WSS vectors from 2D-CINE-3dir.PC and 3D-CINE-3dir.PC is similar although WSS estimations from 2D-CINE-3dir.PC are slightly larger.

**Patient results**

Fig. 10 illustrates the application of WSS estimation based on 3D data in a patient with atherosclerosis and an aortic-plaque at the inner curvature of the proximal descending aorta. Systolic 3D particle trace visualization (A) showed reduced and potentially locally reversed flow at the plaque location (white arrow) which eventually induced low and inverted WSS vectors as well as increased OSI at this location (B, white arrow). Flow and WSS were considerably different compared to more constant wall shear stress in a normal volunteer as shown in Fig. 9. According to the literature, low and oscillating WSS indicate areas susceptible to vascular remodeling and thus at risk for progression of atherosclerotic disease (4,7-10). These results therefore indicate the potential of our WSS estimation strategy to analyze the effects of vascular disease and their impact on the vessel wall.
Fig. 10: 3D blood flow visualization and planar quantification in the descending aorta (DAo) of a patient with atherosclerotic disease. Systolic 3D particle traces (A) originating from an emitter plane near the left subclavian artery demonstrate low and potentially reversed flow (white arrows) distal to the location of a previously detected plaque. Flow and wall parameter quantification revealed slow and clearly retrograde flow velocities at the inner curvature resulting in substantially reduced and even inverted WSS vectors (B, white arrow) at the site of the plaque.

Error Propagation Analysis

Eq. [11] was numerically evaluated and shown to be continuous, periodic and bound within the following limits:

\[
1.18 \leq \alpha_{B-spline} \cdot \Delta l \leq 1.85
\]

Average values between volunteers were taken for \( \Delta l \), area, circumference, SNR and the number of time frames. The average voxel lengths in 2D and 3D were taken for \( \Delta l \).

The results of the error propagation for the velocity, flow and WSS are presented in Table 4.

<table>
<thead>
<tr>
<th></th>
<th>2D-CINE-3dir.PC</th>
<th>3D-CINE-3dir.PC</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNR</td>
<td>42.9</td>
<td>55.5</td>
</tr>
<tr>
<td>( \sigma_v ) [m/s]</td>
<td>0.0157</td>
<td>0.0122</td>
</tr>
<tr>
<td>( \sigma_{flow} ) [mL/s]</td>
<td>0.0821</td>
<td>0.157</td>
</tr>
<tr>
<td>( \sigma_{WSS} ) [N/m²]</td>
<td>0.00217</td>
<td>0.00207</td>
</tr>
</tbody>
</table>

Flow and WSS errors propagated from measurement errors are about 2 orders of magnitude smaller than the physiologically measured Flow and WSS. The propagated errors on Flow and WSS were as well systematically smaller compared to the inter-modality and inter-observer errors.

Discussion:

Quantification of CINE PC-MRI data and WSS estimation is a challenging task because of the limited spatio-temporal resolution, SNR and the difficulty to accurately segment the moving vessel lumens. To date, most approaches consisted of either fitting a restrictive flow model (e.g. paraboloid method (18)) or deriving numerical flow simulations (11,13,14).

The aim of this study was to evaluate a new processing strategy for the direct estimation of axial
and circumferential WSS components and flow parameters from the MR velocity data. The method presented here aims at a direct estimation of such parameters from PC-MRI data by using cubic B-spline interpolation and Green’s theorem. No assumptions other than relative smoothness of the velocity field (continuity up to the second order derivatives) were made. B-spline interpolation was chosen based on its excellent interpolation (38,39) quality in combination with limited computational burden (40-42). Each vessel lumen was segmented using cubic B-spline contour due to their smoothness, flexibility and continuity properties. Additionally, it has been shown that B-spline of cubic order present a minimum curvature property (43) which makes them particularly adequate for segmentation of fluid-solid interfaces (44). Furthermore, the finite difference property of the B-spline model provided analytical velocity derivatives along the segmentation contour, which was of particular importance for the calculation of flow parameters and WSS.

Synthetic data analysis showed that the limited resolution provided by MRI is introducing underestimation in the measurement of in-vivo WSS (about 50% for a WSS of 0.6 N/m²). Flow volume is only slightly underestimated, mainly due to segmentation errors and partial volume effect. The measured WSS is only an estimator of WSS but remains correlated to the actual WSS.

Error propagation analysis showed that PC-MRI measurement errors have only very limited effects on flow and WSS estimations (2 orders of magnitude smaller than the measured parameters).

In-vivo data demonstrated close agreement for flow and WSS between 2D and 3D-CINE-PC. Nevertheless, parameters related to higher spatio-temporal frequencies such as WSS and OSI are more limited by the limited resolution of MRI and 3D-CINE-PC systematically underestimated WSS (relative error of 45%). Note, that the relative errors between 2D-CINE-3dir.PC and 3D-CINE-3dir.PC are not only related to the different spatio-temporal resolutions but are affected by measurement errors or segmentation errors as well, which may explain the higher error level in regards to the predictions from synthetic data. Although WSS values were systematically underestimated in 3D-CINE-3dir.PC, the high consistency between volunteers indicates the potential of WSS estimation for the analysis of relative pathological WSS alterations.

The influence of segmentation error was evaluated by comparing measurements between 2 independent observers. Flow and Area demonstrated small inter-observer variability while the inter-observer variability of WSS remained at reasonable levels (7/18 % median relative error in 2D/3D). The overall smaller inter-observer variability from the 2D data in comparison to the 3D data can be associated with the higher spatial resolution and improved lumen contrast due to inflow effects. The inter-observer variability was assessed using plane 1 in the ascending aorta, which exhibits the most pronounced compliance, i.e. lumen area change, and lumen motion during the cardiac cycle. Segmentation of this plane was consequently the most complicated and the resulting inter-observer errors should be taken as upper boundaries.

Presence of a circumferential component of aortal WSS accounting for 10 - 20% of the total WSS indicate that the vectorial nature of WSS has to be taken into account to fully characterize endothelial function. Moreover, circumferential WSS was linked to the normal hemodynamics in the aorta. Right handed and left handed helical flow in the ascending and descending branches of the aorta resulted in circumferential WSS reaction forces in the same directions. Interestingly, the inter-modality variability between 2D and 3D acquisitions was smaller for the circumferential WSS component than for the WSS magnitude. This might be due to the fact that
the smaller circumferential component was derived from velocities with smaller spatial variations. Consequently, it might be better evaluated even at low resolutions (i.e. low sampling frequencies).

A limitation of this study is related to the identical flip angles used for both 2D and 3D acquisitions. Due to the increased blood saturation for 3D imaging by repeated volumetric rf-excitation, an individual optimization and lower flip angles may have resulted in improved blood SNR and image quality. Future studies should thus include a more detailed MR protocol optimization of the individual data acquisition methods.

Although inter-observer variability and SNR error propagation were analyzed, inter-scan reproducibility was not evaluated within the framework of this study. Due to the long scan times, repeated measurements were not performed during this study and inter-scan variability could not be assessed from the available data. However, considering the very limited effect of finite SNR on the measurement error in comparison to the inter-observer reproducibility, we speculate that the inter-observer variability was the limiting factor regarding reproducibility and thus accounts for most of the inter-scan variability.

The large inter-modality and inter-observer relative errors for OSI seem to be due to the low average OSI levels in young healthy volunteers and are not reflected in the absolute error (below 5%).

Note that although all PC-MRI data underwent eddy current correction, remaining errors due to concomitant and non-linear gradients may still introduce errors in the encoded velocities. Since such imperfections substantially increase with increasing distance from the isocenter of the magnet, distal imaging slices, i.e. in the descending aorta, may be most affected. Such errors may have introduced inconsistencies in the flow estimation, as in slices 6-7-8 for the 2D acquisitions or in slices 1-2-3 for the 3D acquisitions. Considering the already long examination protocol of this study, volunteers were not repositioned between 2D-CINE-3dir.PC acquisitions. Further improvements should therefore include corrections for concomitant gradients and gradient field non-linearity before flow visualization and quantification.

As represented in Table 5, the WSS measurements reported in this study are in good agreement with other published results derived from phase-contrast MRI in the descending and abdominal aorta.

Table 5: Reported WSS values of the descending and abdominal aorta using MRI. Imaging modality is represented as nD-CINE-mdir.PC with n being the imaging dimensionality and m the dimension of the velocity encoding.

<table>
<thead>
<tr>
<th>Study</th>
<th>Aortic branch</th>
<th>Imaging modality</th>
<th>Mean WSS (SD) [N/m²]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stalder et al.</td>
<td>Descending aorta (plane 8)</td>
<td>2D-CINE-3dir.PC</td>
<td>0.56 (0.08)</td>
</tr>
<tr>
<td>Stalder et al.</td>
<td>Descending aorta (plane 8)</td>
<td>3D-CINE-3dir.PC</td>
<td>0.38 (0.08)</td>
</tr>
<tr>
<td>Wentzel et al. (10)</td>
<td>Descending aorta</td>
<td>2D-CINE-1dir.PC</td>
<td>0.36 (0.17)</td>
</tr>
<tr>
<td>Moore et al. (16)</td>
<td>Abdominal aorta suprarenal</td>
<td>2D-CINE-1dir.PC</td>
<td>0.13</td>
</tr>
<tr>
<td>Pedersen et al. (17)</td>
<td>Abdominal aorta</td>
<td>2D-CINE-1dir.PC</td>
<td>0.62 / 0.27</td>
</tr>
</tbody>
</table>
Unlike previously reported methods, the method presented here is based on 3-directional velocity encoding in order to derive vectorial WSS. Three-directional velocity encoding as well as 3D imaging do generate highly valuable additional information compared to 2D techniques, however they come at the cost of longer scan times. The scan times of 10-20 minutes for 4D flow-sensitive MRI (3D-CINE-3dir.PC) may limit the clinical application of the method.

Since the presented WSS estimation method is not based on a circular vessel assumption, it can be applied to more irregular vessel areas such as bifurcations or aneurysms (45). Providing that the velocities measured on a plane transversal to the vessel have sufficient resolution and SNR, the proposed data processing strategy can provide accurate WSS parameters such as regional axial and circumferential WSS or OSI. In highly-stenotic regions, however, MRI can no longer be used to image the vessel lumen or a flow profile in the stenosis with sufficient resolution without major methodological modifications. In general, it is not possible to assess correctly the flow if the vessel diameter in the stenosis has the same order of magnitude as the voxel size. Consequently, WSS estimation in stenotic regions is challenging and may suffer from large numerical errors. However, the presented method may still be useful to evaluate stenosis formation as well as pre- and post-stenotic flow (i.e. the flow proximal and distal to the stenosis) and to estimate WSS in these regions (46). Such data may provide clinically useful information regarding post-stenotic vessel wall alteration and progression of atherosclerotic disease. More generally, WSS is believed to play an important role in the evolution of atherosclerosis and other arterial diseases such as aneurysms for which flow measurements do not present such limitations due to spatial resolution.

Other previously described methods for the estimation of WSS include Computational Fluid Dynamics (CFD). CFD is time-consuming but does not present measurement errors such as PC-MRI and can derive very good WSS estimations from the calculated velocity field. However it remains limited by its assumptions on blood properties, boundary conditions or on vessel wall properties. In addition, CFD based WSS estimations remain difficult and may require extremely small mesh sizes at the boundary layer of the CFD geometries (15). Nevertheless, CFD has proved to be a useful tool in a number of previous studies (11,13,14). While methods based on PC-MRI is limited because of low spatial resolution and SNR, CFD does not have such restrictions but is limited due to the difficulty to accurately model the complex hemodynamics. In this context, a general comparison of flow analysis between CFD and PC-MRI would be of high interest but was beyond the scope of this paper. Initial results of an ongoing study at our institution point to the potential of using both PC-MRI and CFD for a mutual enhancement of the quantification accuracy (47).

At present, an exact measurement of WSS in-vivo remains a yet unresolved challenge however this study was able to provide the first robust and reproducible in-vivo estimation of vectorial WSS in the entire human thoracic aorta.
Appendix:

A. B-spline interpolation

Splines are piecewise and smoothly connected polynomials. For B-splines, the spline function is obtained as a sum of a finite number of basis functions. Since each basis function has a finite support, this is a computationally efficient way of representing splines (41-43).

The classical interpolation problem consists in finding \( f(x) \) \((x \in \mathbb{R})\) given \( f(k) \) \((k \in \mathbb{Z})\), with the interpolating condition that \( f(x)|_{x=k_i} = f(k_i) \). The B-spline solution (41-43) is:

\[
f(x) = \sum_{k \in \mathbb{Z}} c(k) \beta^n(x-k) \tag{[A1]}
\]

with the B-spline basis function:

\[
\beta^n(x) = \frac{\beta^n \ast \beta^n \ast \ldots \ast \beta^n(x)}{(n+1) \text{ times}}
\]

and the coefficients: \( c(k) = \left( (b^n)^{-1} \ast f \right)(k) \).

Note that \( b^n_i(k) := \beta^n(x)|_{x=k} \) can be efficiently calculated using a cascade of 1st order recursive filters (40,42). Of particular interest to the topic discussed here is the finite difference property of B-spline:

\[
\frac{d\beta^n}{dx}(x) = \beta^{n-1}(x+1/2) - \beta^{n-1}(x-1/2) \quad \text{and} \quad \frac{d^2\beta^n}{dx^2}(x) = \sum_{k \in \mathbb{Z}} c(k) \frac{d\beta^n}{dx}(x-k) \tag{[A2]}
\]

i.e.: the derivative of the spline function is analytically computed by simply using another basis function.

Eq. [A1] and [A2] can be rewritten using an interpolating basis function:

\[
f(x) = \sum_{k \in \mathbb{Z}} f(k) \beta^n_{\text{int}}(x-k) \tag{[A3]}
\]

\[
\frac{d^2f}{dx^2}(x) = \sum_{k \in \mathbb{Z}} f(k) \frac{d\beta^n_{\text{int}}}{dx}(x-k) \tag{[A4]}
\]

With \( \beta^n_{\text{int}} = \sum_{k \in \mathbb{Z}} (b)^{-1}(k) \beta(x-k) \)

For cubic splines \((n=3)\), we have:

\[
\beta^3_{\text{int}} = \left( \frac{1-\alpha}{1+\alpha} \right) \sum_{k \in \mathbb{Z}} \alpha^{|k|} \beta^3(x-k) \tag{[A5]}
\]

\[
\frac{d\beta^3_{\text{int}}}{dx} = \left( \frac{1-\alpha}{1+\alpha} \right) \sum_{k \in \mathbb{Z}} \alpha^{|k|} \frac{\partial \beta^3}{\partial x}(x-k) \tag{[A6]}
\]

With \( \alpha = -2+\sqrt{3} \)

B. General formulation of WSS (48)

The general formulation for the stress tensor is given by:

\[
\sigma = \tau + p\tilde{I} \tag{[A7]}
\]

with \( \tau \) : viscous stress tensor, \( p \) : pressure, \( \tilde{I} \) : identity matrix.

While the symmetric second order stress tensor \((\sigma)\) depends on the velocity field and the location only, the surface stress vector \((\tilde{\sigma})\) additionally depends on the orientation of the vessel wall.
\[
\vec{\sigma} = \vec{\sigma} \cdot \vec{n} = \vec{\tau} \cdot \vec{n} + p \vec{I} \cdot \vec{n}
\]

With \( \vec{n} \): inward unit normal

For a Newtonian and incompressible fluid, the viscous stress tensor \( \vec{\tau} \) is given by \( \vec{\tau} = 2\eta \dot{\varepsilon} \), with \( \eta \): viscosity, \( \dot{\varepsilon} \): deformation tensor (see equation [4], Methods). The general form for the wall shear stress (\( \vec{\tau} \)) is then:

\[
\vec{\tau} = 2\eta \dot{\varepsilon} \cdot \vec{n}
\]

Note that if a 1D problem is considered, \( \vec{\tau} \) simplifies to: \( \vec{\tau}_{1D} = \eta \frac{\partial v}{\partial h} \), with \( v \): the velocity and \( h \): the height of the boundary

C. Calculation of WSS from 2D data with 3D velocity encoding

The relation between the WSS vector and the three-directional velocity field is given by:

\[
\vec{\tau} = 2\eta \dot{\varepsilon} \cdot \vec{n} = \eta \left[ 2n_1 \frac{\partial v_1}{\partial x_1} + n_2 \left( \frac{\partial v_1}{\partial x_2} + \frac{\partial v_2}{\partial x_1} \right) + n_3 \left( \frac{\partial v_1}{\partial x_3} + \frac{\partial v_3}{\partial x_1} \right) \right]
\]

In order to calculate \( \vec{\tau} \) from 2D data with three-directional velocity encoding, it was assumed that the 2D analysis plane was normal to the vessel surface, i.e. \( \vec{n} = (n_1, n_2, 0) \). Furthermore, a no flow through the vessel wall was enforced, i.e. \( \vec{n} \cdot \vec{v} = 0 \). This implies:

\[
\vec{n} \cdot \frac{\partial \vec{v}}{\partial x_3} = n_1 \frac{\partial v_1}{\partial x_3} + n_2 \frac{\partial v_3}{\partial x_3} = 0
\]

and finally, equation [A10] reduces to:

\[
\vec{\tau} = \eta \cdot \left[ n_1 \left( \frac{\partial v_1}{\partial x_1} + \frac{\partial v_3}{\partial x_3} \right) + 2n_2 \frac{\partial v_2}{\partial x_2} \right]
\]

which can be used to calculate vectorial WSS from data of transversal planes with three-directional velocity information.
D. Green’s Theorem

The Green’s theorem (49) provides the relationship between a surface integral over a regular domain $D$ and a line integral around the simple and oriented closed curve representing the domain boundary ($\partial D$). For a function $P$ continuous in the domain $D$:

$$\int_{\partial D} P \, dx = - \iint_D \frac{\partial P}{\partial y} \, dxdy \quad [A12]$$

References:


